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THE TREATMENT OF VENTRICULAR SEPTAL DEFECT

BY

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The natural history of ventricular septal defect (V.S.D.) is such that few patients survive past the third decade (Brotmacher and Campbell, 1958). It is therefore fortunate that the introduction of the cardio-pulmonary bypass has permitted effective surgical treatment. This is now current practice in the U.S.A. (Kirklin *et al.*, 1957; Warden *et al.*, 1957; Gerbode *et al.*, 1958). The object of this paper is to present a series of 21 patients with V.S.D.s, operated on under total cardio-pulmonary bypass with the Melrose-N.E.P. pump-oxygenator at Hammersmith Hospital. These patients form the major group of a total of 40 operated on in this way for the correction of congenital cardiac defects during the last 18 months.

The Patients.—The ages of the 21 patients ranged from 2½ to 25 years, the average being 8½ years. Of these patients with V.S.D. four had in addition a patent ductus arteriosus. Of the cases without a duct three were unusual. One had a single ventricle, one had two V.S.D.s, and in one the V.S.D. was in an unusual site in relation to the tricuspid valve (Case 13).

Clinical Picture

Symptoms

Infancy is known to be a hazardous period in patients with large V.S.D.s, and over half of the 320 patients of Keith *et al.* (1958) died before the age of 1 year. Similarly, in our cases there was often a history of feeding difficulties, with breathlessness and cyanosis, and very slow weight gain in infancy. After the age of 1 year they did better, though frequent chest infections were still common, and when seen by us they were often remarkably asymptomatic and active. Dyspnoea on exertion was no more than slight in two-thirds and was severe in only one case (Case 2).

Signs

These children were commonly undersized for their age, being on average 18% below the expected weight. Chest deformity with uniform or asymmetrical bulging of the sternum and Harrison's sulcus was frequently noted (Fig. 7). Clubbing was never seen, but slight cyanosis was occasional and was usually peripheral, the arterial oxygen saturation being always above 88%. No patient had congestive heart failure at the time of operation.

Jugular Venous Pulse.—This was abnormal in eight, consisting usually of a moderately dominant *a* wave; a really conspicuous *a* wave was seen only once (Case 13).

Arterial Pulse.—The volume was usually normal or slightly small and the rhythm regular. A slight-to-moderate waterhammer quality was found in 11. A striking suprasternal arterial pulsation was found in Cases 14 and 15, which had in addition a patent ductus.

Cardiac Pulsation.—The type of pulsation varied according to the size of the left-to-right shunt and the pulmonary resistance. When the shunt was considerable there was a localized hyperdynamic thrust at the apex, indicating left ventricular enlargement, and a diffuse parasternal heave due to enlargement of the right ventricle. When the shunt was smaller and the pulmonary resistance appreciably raised (around 9 units) the left ventricular thrust was less impressive and the dominant pulsation was that of the right ventricle.

Auscultation

V.S.D. Thrill and Murmur.—These were usually maximal at the left sternal edge, and in most cases the murmur was loud and long, indicating a substantial flow through the defect (Fig. 1A). In the patients with a pulmonary resistance of 9 units or more the murmur and thrill were softer and shorter, owing to reduction in flow through the defect (Fig. 1C).

Apical Diastolic Murmur.—A low-pitched delayed murmur at the apex attributed to a torrential mitral blood flow (Wood, 1956) was heard in all cases. When loud and long the left-to-right shunt was always large (Fig. 1A). We expected, when the murmur was soft and short, that the shunt would be small and the resistance high, but this was not always so. Of the six cases with this type of murmur, four had a large shunt and in two the shunt was small.

Basal Diastolic Murmur.—An early blowing diastolic murmur was heard in the left second to third spaces in eight patients. At operation three were shown to have a ductus, one was proved to have aortic incompetence, and one to have pulmonary incompetence. The cause

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of the murmur was not determined in the remaining three and disappeared after operation in one. In these three it was presumed to be due to aortic or pulmonary incompetence.

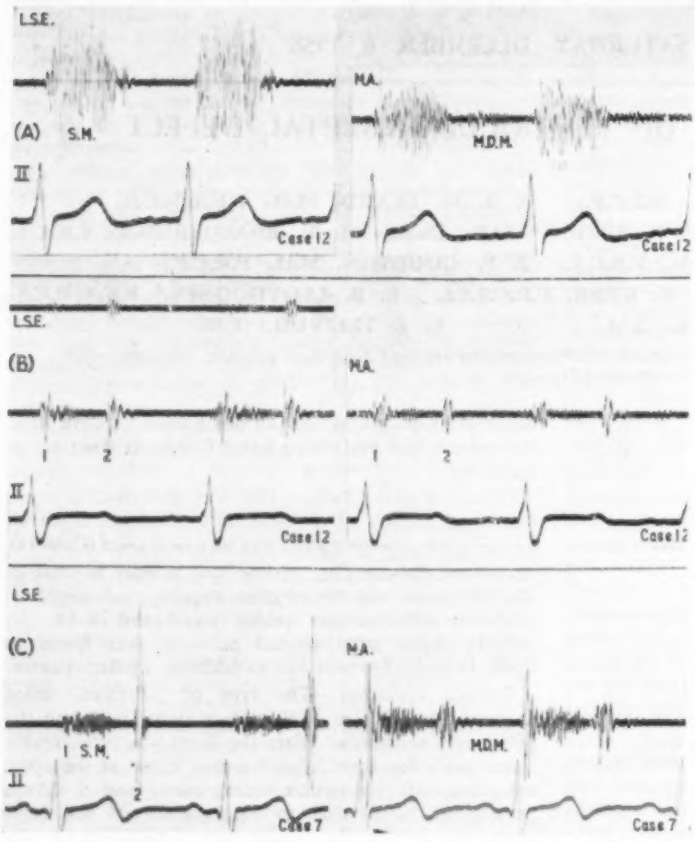

FIG. 1.—Phonocardiograms taken at the left sternal edge (L.S.E.) and at the mitral area (M.A.). (A) Loud long systolic murmur (S.M.) and long mitral diastolic murmur (M.D.M.) in a patient with a large left-to-right shunt and low pulmonary resistance. (B) Same patient as (A) showing disappearance of significant murmurs after closure of defect. A soft ejection systolic murmur is shown. Note appearance of right bundle-branch block. (C) Short soft systolic murmur in a patient with only a small left-to-right shunt and high pulmonary resistance. The second heart sound is very loud and virtually single, and the mitral diastolic murmur is soft and short.

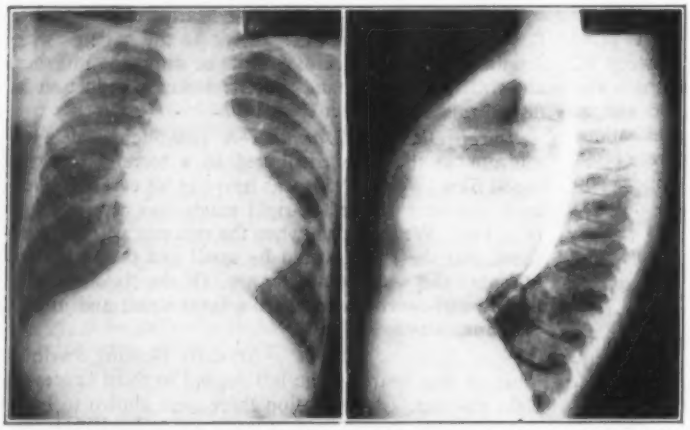

FIG. 2.—Postero-anterior and lateral views of the heart in Case 4 with a large left-to-right shunt and only slightly elevated pulmonary resistance. The right ventricle and pulmonary artery are enlarged and there is pulmonary plethora. Definite left atrial enlargement is seen in the lateral view.

Second Heart Sound.—This was loud and narrowly split in all patients except three. One of these was found to have definite organic pulmonary valve stenosis at operation, one had aortic incompetence and infundibular obstruction and the other (Case 13) had an unusual defect, referred to later.

Other Sounds.—Two cases had a pulmonary ejection click and high pulmonary pressures, but with a substantial shunt. An ejection click at the apex, thought to be aortic, was heard in one patient who had also a patent ductus. No other abnormal sounds were heard in any patient.

Associated Non-cardiac Anomalies

These were usually absent, but one patient had stigmata of the "rubella syndrome" and also a patent ductus. Another patient had right basal bronchiectasis.

Methods of Study

Radiology

The heart was enlarged in every case, being usually moderate in degree with a cardio-thoracic ratio of 55–65%. Enlargement was considerable in two and slight in three. Both ventricles were enlarged in every case. The left ventricle tended to be less prominent in the cases with a high pulmonary resistance. Left atrial enlargement, of slight-to-moderate degree, was present in all save two, of whom one had substantial infundibular stenosis and the other a high pulmonary resistance (14 units). Impressive right atrial enlargement was seen only twice. One of these patients (Case 13) appeared at operation to have tricuspid incompetence; in the other patient (Case 21) clockwise cardiac rotation was found at operation.

Enlargement of the main pulmonary artery was invariable, as was plethora of the lung fields. Intrinsic pulsation of the small branches was well marked in all. The size of the aorta was unremarkable.

Fig. 2 shows the radiological features in a typical case.

Aortography was performed on two patients and one was shown to have a patent ductus (Case 20).

Electrocardiography

Right atrial P waves were found in six cases and were gross in only one (Case 13). Left atrial P waves occurred in 11. Direct evidence of right ventricular hypertrophy (Hollman, 1958) was found in 11, and 7 of these had an RSR pattern in VI and one had complete right bundle-branch block. Direct evidence of left hypertrophy (Cabrera and Monroy, 1952) consisting variously of deep Q waves, tall R waves, or tall peaked T waves was found in 19 (Fig. 3).

Lone right hypertrophy was found in only one (Fig. 4), while solitary left hypertrophy occurred in six. Thus 14 patients had combined hypertrophy. In six of these the right ventricle appeared dominant and in three the left. We had expected that when the left ventricle dominated the

right the pulmonary flow would be higher and the resistance lower than when the right ventricle was dominant. This was not the case, for there was no clear relationship between the cardiographic and haemodynamic findings. Further, it was anticipated that when the right ventricle dominated the left a smaller fall of right heart pressure would occur than when the left ventricle was dominant, but we were disappointed in this also. Nevertheless we continue to use the cardiogram in the assessment of individual patients in the belief that the presence of left hypertrophy is a favourable sign.

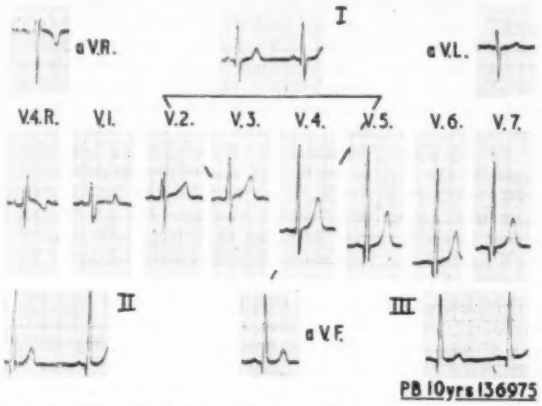

FIG. 3.—Electrocardiogram of Case 19, showing dominant left ventricular hypertrophy with deep Q waves, tall R waves, only small S waves, and tall T waves in V5–V7. Slight right ventricular hypertrophy is present too.

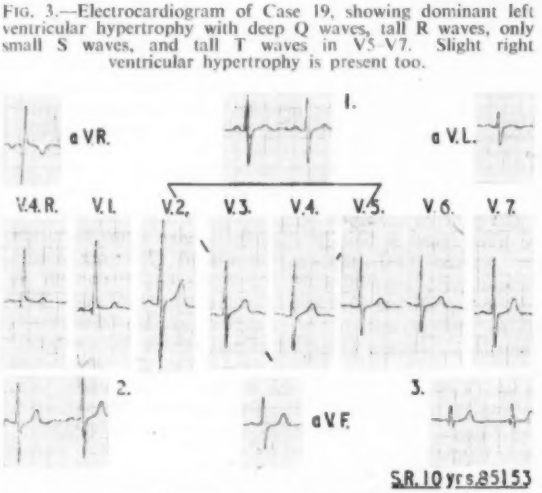

FIG. 4.—Electrocardiogram of Case 1 showing dominant right ventricular hypertrophy with no clear evidence of left ventricular hypertrophy at all. There is a monophasic R wave in V1 with S waves across to V7 and a dominant R wave in lead aVR. There are no Q waves in V5–V7.

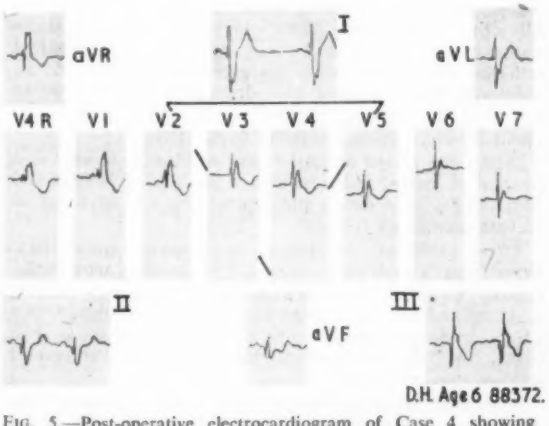

FIG. 5.—Post-operative electrocardiogram of Case 4 showing complete right bundle-branch block with the secondary R wave present even in V7. Well-marked T-wave inversion is present across to V5.

Cardiac Catheterization

This was carried out in every case, and the data were used to estimate the size of the defect, the severity of the pulmonary vascular disorder, and the presence of associated anomalies. The size of the left-to-right shunt was expressed as the ratio of pulmonary to systemic flow.

$$\frac{\text{Pulmonary flow}}{\text{Systemic flow}} = \frac{\text{Systemic A–V } O_2 \text{ difference}}{\text{Pulmonary A–V } O_2 \text{ difference}}$$

The pulmonary arteriolar resistance was expressed in arbitrary units (Wood, 1956), and in cases where the oxygen consumption was not measured an average value for age and surface area was obtained from tables.

The results of this investigation are summarized in Table I.

TABLE I.—*Haemodynamic Studies at Catheterization, at Operation, and Results*

Case No.	Age	Pulmonary Artery Pressure (mm. Hg)	Pulmonary Systemic Flow Ratio	Pulmonary Arteriolar Resistance (Units)	% Fall in R.V.P.† / L.V.P.	Result
			V.S.D. Alone			
1	10	100/57	1·5	9	37	Dead
2	2½	39/12	5·0	3*	6	Alive and well
3	5	100/35	1·8	13*	65	" " "
4	5	70/20	2·0	4	9	" " "
7	7	75/55	1·1	17*	2	" " "
8	7	70/40	2·2	6*	41	" " "
10	10	83/48	2·0	6	58	" " "
11	8	120/70	2·0	9	44	" " "
12	10	60/30	2·4	3·5*	37	" " "
13	9	42/20	2·5	1·5	13	" " "
16	4½	75/40	2·7	9·5*	54	" " "
17	9	55/20	1·8	5*	8	" " "
18	25	17·5	4·5	1*	55	" " "
19	11	32/8	3·2	1·5*	31	" " "
21	13	44/8	2·6	1·5	16	" " "
			V.S.D. and Patent Ductus			
5	3½	40/20	2·8	1*	27	" " "
14	10	110/60	2·0	20*	5	Dead
15	9	70/53	1·3	18*	—	"
20	3½	60/20	3·7	4·5*	28	Alive and well
			Two Ventricular Defects			
9	2½	72/20	2·6	10*	0	Dead
			Single Ventricle			
6	7	75/30	2·0	5	0	Alive and well

* O_2 consumption assumed.
† R.V.P. = right ventricular systolic pressure. L.V.P. = left ventricular systolic pressure.
% fall in $\frac{\text{R.V.P.}}{\text{L.V.P.}}$ $\frac{\text{R.V.P.}}{\text{L.V.P.}}$ % before closure minus $\frac{\text{R.V.P.}}{\text{L.V.P.}}$ % after closure.
Also see text.

The pulmonary artery pressures ranged from 17/5 to 120/70, and were mostly of the order of 70/50 mm. Hg. The left-to-right shunt was large in all but three cases, the ratio of pulmonary to systemic flow ranging from 1.1:1 to 5:1, with an average of 2.4:1. The pulmonary resistance was usually only moderately elevated, but in four patients it was high. The average for all cases was 7.4 units. An infundibular gradient, usually slight, was found in nine patients and ranged from 7 to 40 mm. Hg. One patient had a 30 mm. Hg gradient at valve level. The oxygen saturation was higher in the pulmonary artery than the right ventricle in four patients, of whom two had an associated patent ductus. In two cases proved to have a ductus the saturation in the two sites was equal. The arterial oxygen saturation was always above 88%, and averaged 93%.

The pulmonary wedge pressure when determined ranged from 5 to 16 mm. Hg (measured from 5 cm. below the sternal angle).

Associated Lesions and Unusual Features

Patent Ductus Arteriosus.—The classical signs were absent, although suspicion was raised by an early diastolic murmur at the left sternal edge in two. Cardiac catheterization

revealed a further rise in oxygen saturation in the pulmonary artery as compared with the right ventricle in only two, even though in another the ductus was found at operation to be large and the ventricular defect small. On *x*-ray examination the pulmonary artery was always at least moderately dilated. Our experience indicates that when the ductus is patent in the presence of a V.S.D., it is difficult to diagnose pre-operatively with certainty without the aid of retrograde aortography. The importance of the patent ductus in relation to perfusion is discussed below. Patency of the ductus should be suspected if there is a basal early diastolic murmur, if the catheterization data suggest a further left-to-right shunt at pulmonary artery level, or if there are any other features associated with patent ductus, as in one of our patients who had stigmata of the "rubella syndrome" (Heiner and Nadas, 1958).

Obstruction to Right Ventricular Outflow.—Nine patients were found to have infundibular obstruction at cardiotomy, while another had definite valvular stenosis. In no case was the obstruction severe enough to reverse the left-to-right shunt, and the pulmonary artery pressure was elevated in all but one.

Pulmonary Valve Lesions.—Two patients had abnormal valves. In Case 5 the cusps were fused and the orifice reduced to 1 cm. in diameter. In Case 18 the cusps were adherent to the pulmonary ring, and this gave rise to pulmonary incompetence with a diastolic thrill.

Atypical Ventricular Defects

Case 6.—This boy of 7 years with a *single ventricle* was of exceptional interest, for pre-operatively all the signs were those of a straightforward ventricular defect apart from the cardiogram. This showed gross left-axis deviation with extreme clockwise rotation and absent Q waves over the left ventricle.

Case 9.—This patient, a girl aged 2½ years, had *two ventricular defects*, and pre-operatively the only hint of an associated lesion was a very large diphasic complex in lead I of the cardiogram.

Case 13.—In this girl of 9 years the defect was a low one beneath the septal cusp of the tricuspid valve, and the jet from the left ventricle was directed partly into the right atrium. Clinically the patient was unusual because she had a tall *a* wave, a widely split second sound, a very large right atrium, and the systolic thrill was near the apex.

Indications and Contraindications to Operation

In view of the known poor prognosis it is clear that all patients with a moderate-sized or large defect should be considered for surgery unless there is some contraindication. It is equally clear that the main hazard regarding closure is the presence of severe pulmonary vascular disease, because patients with this complication have a very high operative mortality and also may derive uncertain benefit if they survive. Thus the difficulty in selecting suitable cases for operation is experienced mainly in those patients who have an elevated pulmonary vascular resistance.

If the pulmonary resistance is so high as to cause an obvious right-to-left shunt with an arterial oxygen saturation below 85%, with or without cyanosis and clubbing, then closure of the defect should not be recommended. Such cases will have only a small left-to-right shunt with pulmonary flow less than 1.5 times the systemic, and the clinical features previously mentioned of a substantial shunt will be absent. The whole clinical picture, in fact, will be dominated by evidence of extreme pulmonary hypertension.

Cases less severe than this first group but with a substantially elevated pulmonary resistance (9 units or more) present the greatest difficulties in selection and a careful consideration of *all* aspects of the patient is essential. It is doubtful whether any one parameter is of overriding importance. Evidence for the presence of an appreciable left-to-right shunt with only a small or absent right-to-left shunt must be sought, so that a fall in pulmonary artery pressure after closure can be anticipated.

Case 3 can be cited as an example of a patient in this group, for she had a pulmonary artery pressure of 100/35 mm. Hg and a pulmonary arteriolar resistance of 13 units. We were encouraged to operate on her by finding a definite left ventricular thrust at the apex even though the right ventricular pulsation was prominent too, by a long loud V.S.D. murmur and thrill with a moderately loud mitral diastolic murmur, by the presence of a qR pattern in V6 even though R was monophasic in V1, and by a pulmonary flow 1.8 times the systemic. At operation a good drop in pulmonary artery pressure after closure was obtained. On the other hand, a girl of 9 with a pulmonary artery pressure of 80/40 mm. Hg and a pulmonary resistance of 14 units was thought to be unsuitable because of the following features. Clinically the left ventricle was doubtfully palpable, the V.S.D. murmur was not full length, and the thrill rather weak, there was no mitral diastolic murmur, the cardiogram showed deep S waves with no Q waves over the left ventricle, and the pulmonary flow was only 1.2 times the systemic.

The ideal case for operation is typified by Case 12. This boy of 10 years had a pulmonary resistance of 3.5 units, with a pulmonary artery pressure of 60/30 mm. Hg and a pulmonary blood flow 2.4 times the systemic. Clinically there was a quite forceful localized thrust at the apex, a loud long V.S.D. murmur with a strong thrill, and a loud long mitral diastolic murmur. The cardiogram showed a small Q, tall R, and small S in V6 with a prominent peaked T wave, and the predominant deflection in aVR was negative. On *x*-ray examination he had well-marked pulmonary plethora. At operation his pulmonary artery pressure dropped from 50/20 to 27/20 mm. Hg after closure of the defect.

Anaesthesia

The patients are made very drowsy by premedication, and we have found it best in children to give quinalbarbitone per rectum (4–5 mg./kg., maximum 200 mg.) with intramuscular promethazine (1.5–2 mg./kg., maximum 50 mg.) and pethidine (3–4 mg./kg., maximum 100 mg.). This allows the patient to be weighed without disturbance immediately before induction of anaesthesia by a minimal dose of thiopentone (25–50 mg.). After curarization (tubocurarine 0.5 mg./kg.) the trachea is intubated. Very light general anaesthesia is maintained with nitrous oxide and oxygen, using intermittent positive-pressure ventilation by a pulmoflator.

In the theatre a cannula is placed in a left arm vein for blood transfusion; a nylon catheter is passed from a right arm vein into the thorax for measurement of superior vena caval pressure and serves as an alternative route for intravenous therapy. Blood lost during surgery is estimated by weighing swabs and measuring suction loss, continuous balance being maintained by transfusion with citrated blood. All other intravenous fluids, including those used in manometry, are restricted to a minimum. Intermittent pethidine and tubocurarine are given as needed, with an additional dose of these two drugs before perfusion to anticipate the sudden dilution of circulating anaesthetic agents by blood from the pump oxygenator.

During the period of total bypass the lungs are held in a position of partial inflation with a mixture of helium and 20% oxygen at a steady pressure of 5–8 cm. of water to prevent pulmonary collapse.

After perfusion, ventilation is resumed with 100% oxygen until nitrous oxide is needed to maintain anaesthesia. Usually no more anaesthetic drugs are given; 18 patients spoke as soon as the endotracheal tube was removed, two others gradually returning to full consciousness in two hours. In only one instance was it necessary to reverse residual curarization.

Bronchial secretions have not been increased and aspiration has been unnecessary, but before the end of the operation a Ryle tube is passed through the nose to empty the stomach and is left in place.

Surgical Technique

Approach to the Heart and Great Vessels.—A vertical sternum-splitting incision is made, using a Gigli saw to divide the bone in the midline. The left internal mammary artery is isolated and catheterized with a fine elastic nylon tube for arterial pressure recording. After reflection of the lower pole of the thymus the pericardium is opened vertically in its full extent. Traction sutures hold the pericardium over the edges of the sternum, thus protecting the pleural cavities. A self-retaining retractor spreads the incision. Whilst the heart is being exposed the left common femoral artery is prepared for later cannulation, and through the same incision in the groin the saphenous vein is catheterized for recording pressure in the inferior vena cava.

Examination of the Heart.—Confirmation of the diagnosis is next sought by direct observation of the size of the various cardiac chambers, by palpation of the thrill invariably present, and by measurement of the pressures within the pulmonary artery and the right and left ventricles. A search is also made for any anomaly in the venous return of the heart, particularly for a left superior vena cava, which if present is temporarily occluded. A most thorough search is made for a patent ductus arteriosus, which must be ligated.

Preparations for Cardio-pulmonary Bypass

Half-inch lengths of Paul's tubing are placed around the venae cavae close to their points of entry into the right atrium and are threaded through a rubber tube to form a snare. The ascending aorta is mobilized at a point approximately 2.5 cm. above its origin so that it will later be possible to occlude it by a clamp put across it at this site. Just proximally a purse-string suture of 5/0 silk is placed through the adventitia of the aorta on its anterior aspect. At this stage heparin (3 mg./kg. body weight) is given. A stainless-steel cannula is inserted into the previously prepared site in the common femoral artery, and this is then connected to the arterial line of the pump oxygenator. Each vena cava is cannulated via separate incisions in the wall of the right atrium in the region of the appendage. The tips of the plastic catheters used are positioned to lie approximately 3 cm. beyond the snares, and they are then joined by a Y connexion to a single tube of 1.25 cm. bore which leads to the oxygenator. The caval catheters are of such a size that flow of blood around them to the heart is not obstructed, but they are known to be more than adequate to carry the flow required during bypass. Care is taken to remove all air from arterial and venous pipelines. Elective cardiac arrest (Melrose *et al.*, 1955; Gerbode and Melrose, 1958) is induced in all cases, and the arresting solution (potassium citrate 1 g. in 50 ml. of blood) is made ready at this stage.

Cardiac Bypass and the Intracardiac Procedure

Partial bypass of the heart and lungs is now begun; the clamps previously applied to the arterial and venous pipelines are removed and venous blood flows by gravity into the oxygenator, arterialized blood being returned by the pump into the femoral artery. Stay sutures are inserted into the right ventricle. A few minutes later a partial bypass is made total by tightening and anchoring the snares around the venae cavae; all blood returning to the heart is thus diverted by the oxygenator, and the heart is seen at once to become much smaller. A small incision is made in the right ventricle between the stay sutures and a low pressure sucker inserted into its cavity; the blood that is aspirated consists of the coronary venous return to the right atrium and the blood returning to the heart from the lungs. Blood sucked in this way is eventually returned to the oxygenator. A needle (18 S.W.G., 8 mm. in length) is next inserted into the lumen of the ascending aorta in the centre of the purse-string stitch, the aorta is then cross-clamped just distally, and the arresting solution injected as rapidly as possible. Within a few seconds cardiac arrest occurs, the needle is withdrawn and the purse-string suture tied to avoid later troublesome bleeding from the puncture site. The ventricular incision is now extended upwards and downwards and the interior of the right ventricle is inspected. The low-pressure sucker is placed in the pulmonary artery after securing a dry field.

The common type of septal defect which lies immediately below the crista supraventricularis can usually be readily identified and adequately displayed for precise closure if traction sutures are inserted at each end of it. The flaccid condition of the arrested heart greatly facilitates the exposure. The defect is closed in two layers by interrupted sutures of silk; care is taken to avoid damage to the leaflets of the aortic valve. When considered necessary for security the second layer of sutures are tied over a small piece of polyvinylformol ("ivalon") sponge. (A very large defect may require insertion of a patch of the same material, as in Case 6.) The rest of the septum is examined for the presence of a second defect, particularly inferiorly in its muscular part. If infundibular narrowing is present sufficient muscle is resected to ensure that there is no

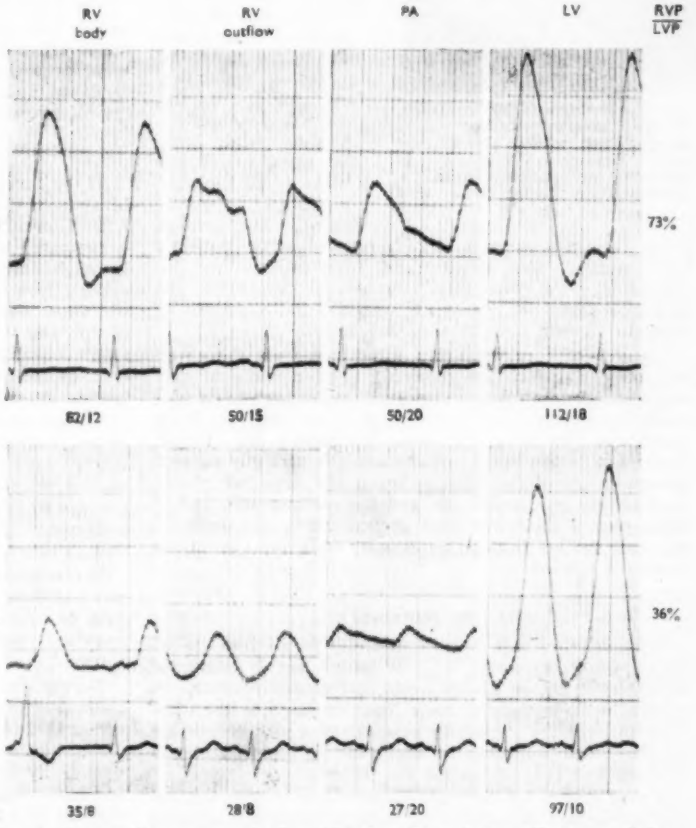

FIG. 6.—Intracardiac pressures in Case 12 before (B) and after (A) closure of the ventricular septal defect. Prior to closure there is a well-marked gradient at infundibular level. After closure of the defect and infundibular resection the gradient is much reduced. Note also satisfactory fall in pulmonary artery pressure.

obstruction to the outflow tract of the right ventricle (Fig. 6). Distension of the left atrium or left ventricle must be prevented at all costs. If bronchial flow is at all great the infundibulum must be resected before closure of the defect. In the presence of an excessive reflux of blood into the left ventricle through an incompetent aortic valve care is taken to prevent distension of this chamber by direct drainage through the left atrial appendage and mitral valve.

The incision in the right ventricle is next sutured, leaving the closure incomplete centrally where the original stay sutures were inserted. The aortic clamp is released; a coronary blood flow thus begins again and the arresting solution is washed out of the myocardium. The blood that initially wells up through the incompletely sutured ventricular incision is discarded, as it is rich in potassium citrate, but after about 15 seconds the low-pressure sucker is reintroduced into the ventricle and the coronary return collected and passed on to the oxygenator. Within one to three minutes cardiac contractions begin, and, as soon as it is found that the beat is powerful enough to eject blood into the aorta against the pressure maintained in it by the pump, the sucker is withdrawn and suture of the ventricle completed. A short while later the caval snares are released and a partial bypass is re-established. The arterial inflow from the pump is steadily reduced as the patient's heart resumes full activity and responsibility for the circulation. At this stage intracardiac pressures are measured again and compared with the initial figures in order to confirm correction of the defect.

FIG. 7.—Photograph of boy (Case 16) two weeks after operation, showing the median sternotomy scar. The chest deformity, so common in patients with a ventricular septal defect, is also well seen.

Closure.—The catheters are withdrawn from the cavae and the atrial incisions repaired. The cannula is also removed from the femoral artery and the incision in its wall carefully repaired. Protamine sulphate (4.5 mg./kg. body weight) is now given in order to restore the clotting mechanism of the blood. Haemostasis is carefully secured before closure of the chest is begun and tubes are placed to drain the pericardial sac and the mediastinum, and if either pleural cavity has been opened this is also drained; all tubes are led through underwater seals and continuous suction is applied.

The Perfusion

The perfusion was without difficulty in all but one of these patients in whom a large patent ductus arteriosus which could not be ligated made perfusion impossible. A patent ductus is a direct route from the aorta to the open heart through the pulmonary vessels, and a high proportion of the blood delivered to the aorta is returned to the machine and fails to perfuse the patient.

A flow rate of 2.4 litres per square metre of body surface was maintained throughout the bypass, which flow allowed but little variation in arterial and venous pressures. The smallest patient received 1.2 litres a minute, the largest 4.3 litres a minute.

The average perfusion was of 39 minutes (30–68 minutes), during which time elective cardiac arrest was maintained for an average of 24 minutes (13–52 minutes).

Venous drainage was obtained by gravity, a difference of 25 cm. (10 in.) being established between the height of the operating table and that of the oxygenator. This differential was always in excess of that required, and on every occasion a screw clamp on the outflow tube had to be partially closed to maintain a normal venous pressure within the great veins. Great care was taken to adjust this clamp accurately, it being felt that such adjustment gives the least possible disturbance to vascular tone and ensures a smooth perfusion.

Return of oxygenated blood into the common femoral artery was always carried out at a line pressure of less than 200 mm. Hg. This pressure, reflecting as it does both the resistance of the cannula and that of the patient's vascular bed, can be used to measure the flow rate from the pump. As the mean pressure in the aorta is known, then the pressure created by the cannula can be determined. Previous calibration of each cannula enables an accurate measurement of flow rate to be obtained from this pressure measurement.

Oxygenation was always adequate, as was carbon dioxide removal. At no time was the rotational speed of the oxygenator excessive, and usually it was below 50 revolutions a minute. Heat loss from the oxygenator was prevented by radiant-heat lamps and the body temperature maintained within 1° C.

Removal of blood from the open heart was never a problem, cross-clamping the aorta producing an almost dry field. Blood contained in the heart at any time was removed by gentle suction and stored in a settling helix before return to the heart–lung machine. An additional high-vacuum suction was available, but blood recovered in this manner was rarely re-used. The pressure in the superior and inferior venae cavae as well as intra-aortic pressure was continuously displayed and recorded. Both the electrocardiogram and the electroencephalogram were similarly monitored.

Post-operative Care

At the conclusion of the operation the patient is carefully lifted from the operating table on to a weighing machine. After allowance for drainage-tubes and dressings his weight is compared with the pre-operative figure. The difference in weight forms a useful check on blood and fluid balance derived from swab-weighing and measurement during the operation. The patient is placed on his bed in the operating theatre and transferred to the recovery ward. An oxygen tent, adequately cooled and humidified, is placed around the head of the patient, and tubes are reconnected to drainage bottles and continuous suction at 3 cm. of Hg vacuum.

A clear record is kept, on which blood transfusion is shown balanced against drainage from pleural and pericardial cavities, and watery fluids infused are balanced against urinary output and gastric aspirations. It is our practice to limit fluid for the first 24 hours to avoid gastric distension. The Ryle tube is aspirated intermittently for the first 24 hours, should nausea or gastric distension warrant it.

Intravenously dextrose 5% with sodium chloride 0.3% is given, 400 ml. per square metre of surface area during the first 24 hours and 800 ml. per square metre during the second 24 hours. Thereafter normal diet is quite rapidly resumed.

During the first 24 hours pulse and blood pressure are charted at 15-minute intervals and the patient is turned and encouraged to cough and breathe deeply. It is found useful to introduce the younger child to an oxygen tent pre-operatively so that his post-operative surroundings are not too unfamiliar. Parents are invited to visit the children as soon as they are in the recovery ward and every few hours thereafter.

Post-operative Drugs.—If the patient has been already digitalized pre-operatively this is continued. Otherwise

digitalis is withheld unless the pulse rate is unduly rapid or the jugular venous pressure high. If heart block is present isoprenaline is administered as a suppository (2.5 mg.) should the heart rate fall below a figure at which a satisfactory blood pressure can be maintained. The precise figure cannot be stated, as the age and condition of the patient is the determining factor. In the two patients in this series who required this drug its use was continued at lengthening intervals from five-hourly for the first 48 hours. Antibiotics, consisting of penicillin, streptomycin, and chloramphenicol, are used prophylactically for the first four days. Some patients received erythromycin and novobiocin, but these drugs were not well tolerated.

Convalescence.—The patients were allowed up at the end of a week and were usually discharged from hospital at the end of three weeks. A number of patients had a rise in jugular venous pressure during the first week post-operatively, but this fell gradually during the last ten days in hospital. These children tend to be extremely active during the last week and can make a marked contrast with the pre-operative picture.

Post-operative Complications

Chest haemorrhage was a problem in only two patients. In all cases the clotting mechanism has been rapidly restored to normal; the platelets have been reduced at the end of the perfusion to an average of 60,000 c.mm., but the figure rises to normal early in the post-operative period. The usual blood loss has been less than 500 ml. In two patients the loss was over 1 litre and probably contributed to their death. Both were patients in whom a fall in pulmonary artery pressure had not been obtained, so that pressures on the right side of the heart were unusually high. It is possible that bleeding may have occurred from manometric puncture sites or the cardiac wounds.

Pulmonary Complications.—Coughing and deep breathing is not easy during the first few post-operative days, though we believe it is less difficult if the midline sternum splitting incision is used. In several of our cases expectoration of sputum has been a problem, but in only one instance was a tracheostomy required. The left lower lobe requires an especially careful watch as it is somewhat displaced by the enlarged heart, and the left main bronchus is often narrowed by the large pulmonary artery. Pulmonary oedema has not been encountered.

Infection.—Localized wound infection occurred in two patients, but in no instance was there any suggestion of infection of the blood stream.

Heart-block.—Transient heart-block has occurred in several patients during the period immediately following re-establishment of the heart-beat. Complete heart-block persisted in two patients, in one of whom the idioventricular rate was too low to support an adequate blood pressure even after intravenous isoprenaline in repeated doses of 0.1 mg. The artificial pacemaker connected directly to the ventricle maintained a satisfactory rate and blood pressure until the child's sudden death 10 hours post-operatively (Case 9). In the other patient the use of isoprenaline was satisfactory.

Surgical Pathology

Septal Defect.—In all patients the right ventricle was grossly enlarged, with a well-marked thrill best felt over the outflow tract and the base of the pulmonary artery. The right atrium was normal in size in all cases except one; in this latter instance the jet of blood passing through the defect was blowing the septal cusp of the tricuspid valve back into the atrium, producing tricuspid incompetence (Case 13). In all our patients the defect was located high up on the septum but inferior to the crista supraventricularis; the upper margin of this defect was formed by the annulus of the aortic valve, with the right and posterior aortic leaflet visible immediately beyond the rim. The lower margin of the defect was formed by the muscular interventricular septum, but often had a well-developed fibrous rim. One patient (Case 9) had in addition a second defect in the muscular septum, and in Case 6 there was a single ventricular chamber. Excluding this last case, the size of the defect varied from 1 to 3.5 cm. in diameter.

Coexistent Patent Ductus Arteriosus.—In our first patient a patent ductus was not suspected until perfusion was started and a shunt from the systemic circulation into the pulmonary artery was encountered. Perfusion proceeded normally after ligating the duct. In all subsequent patients the left pulmonary artery was deliberately explored from inside the pericardium in order to exclude the presence of a ductus, and in this way two further undiagnosed ducts were discovered. One of these was successfully ligated, but the other, a thin-walled friable ductus 2.5 cm. in diameter, tore during mobilization and led to death (Case 15). The ductus diagnosed by aortography (Case 20) was ligated without difficulty.

Infundibular Obstruction.—This was present to some degree in nine of the cases. In all cases the obstruction was due to an irregular but generalized hypertrophy of the muscle of the outflow tract and the crista supraventricularis which appeared to be part of the generalized right ventricular hypertrophy. As much infundibular muscle was removed as was necessary to relieve the obstruction, and post-operative manometry rarely revealed a gradient or more than 10 mm. Hg.

Results

Mortality

Of the 15 patients with a ventricular defect as the sole lesion only one died. Among the four patients with an additional patent ductus, two died. A patient with two defects also died, but one with a single ventricle survived.

As previously mentioned, one of the deaths occurred on the table when it was found impossible to ligate a large ductus. The other three occurred between 5 and 36 hours after operation, and were of a similar pattern with sudden cessation of respiration after a period of restlessness and low blood pressure. None of these patients had more than a slight fall in pulmonary artery pressure after closure of the defect, and it seems possible that death was due to abrupt right ventricular failure. Two of these three had a moderate-to-large haemothorax, one of which was treated by open operation.

Reduction in Right Heart Pressures with Closure

We consider that a substantial fall in right ventricular and pulmonary artery pressure after closure of the defect is an important sign, since it indicates that much of the pulmonary hypertension was due to flow rather than to changes in the pulmonary vessels and therefore that the long-term results from closure of the defect are likely to be good. It also indicates that the defect is substantially closed and that no other lesion causing a further left-to-right shunt—such as a second V.S.D.—is present. In order to take account of changes in systemic pressure after closure we have expressed the right ventricular systolic pressure as a percentage of the left (R.V.P./L.V.P.%), and these pressures have been measured at operation in all cases. Prior to closure, R.V.P./L.V.P. ranged from 37 to 100%, with an average of 67%.

After closure of the defect the right ventricular pressure fell in 16 patients and was unchanged in 4. The extent of the fall has been expressed as R.V.P./L.V.P.% before closure minus R.V.P./L.V.P.% after closure—for example, before 100%, after 63%, fall = 37%. The fall in pressure averaged 33%, with a range of 8 to 58%. Details are available in Tables I and II. A small fall in pressure does not imply a poor result if the initial pressure, as in Cases 2 and 4, is low, but otherwise it presumably indicates that considerable pulmonary vascular disease is present.

In the whole group of 20 patients whose defects were closed the R.V.P./L.V.P.% after closure was close to normal in five, slightly elevated in eight, moderately raised in three, and high in four.

TABLE II.—*Operative Findings, Anatomical and Haemodynamic*

Case No.	Size of Defect (cm.)	Infundibular Hypertrophy	Infundibular Gradient, mm.Hg		R.V.P. %/L.V.P. %*	
			Before	After	Before	After
			V.S.D. Alone			
1	3 × 2	0	0	0	100	63
2	1·5 × 1·5	0	0	0	37	31
3	1·5 × 1	0	25	5	94	29
4	2 × 1	+	50	2	38	29
7	1·5 × 1·5	+	16	6	74	72
8	2 × 2	+	36	10	86	45
10	2·5 × 2·5	0	3	10	92	34
11	3 × 3	+	25	17	83	39
12	3 × 2	+	32	7	73	36
13	1·5 × 1·5	+	7	0	51	38
16	2·5 × 2·0	0	0	0	100	46
17	1 × 1	0	0	5	63	55
18	3·5 × 3·5	+	70	4	100	45
19	2 × 2	+	14	10	70	39
21	2 × 1·5	+	20	15	71	55
			V.S.D. and Patent Ductus			
5	2 × 1·5	0	0	0	67	40
14	2 × 2	+	10	20	91	86
15	0·7 × 0·7	—	—	—	—	—
20	1 × 1	0	0	9	93	66
			Two Ventricular Defects			
9	(1) 1 × 1 (2) 1 × 1	0	0	0	75	96
			Single Ventricle			
6	3·5 × 3	0	12	14	96	96

* $\frac{\text{R.V.P.}\%}{\text{L.V.P.}\%} = \frac{\text{right ventricular systolic pressure}\%}{\text{left ventricular systolic pressure}\%}$

Post-operative Assessment

On discharge from hospital three to six weeks after operation all the patients were active and well. The exercise tolerance was improved in most patients. This was particularly obvious in a boy of 2½ years with a huge left-to-right shunt (Case 2), who from being unable to walk more than 20 yards was able to run vigorously without distress. In one patient (Case 7) who had a very small shunt with a high resistance, and no fall in right heart pressures after closure, there was but little improvement.

The jugular venous pressure and pulse were normal in all except the patient with a single ventricle in whom a high venous pressure persisted for several weeks. The arterial pulse sometimes retained its waterhammer quality and one patient still had complete heart-block, with a rate of 90. The cardiac impulses were usually less marked after operation, but the diminution in right ventricular heave depended on the fall in right ventricular pressure obtained.

The most striking change in physical signs was, however, found on auscultation. The thrill and murmur of the ventricular defect disappeared in all patients (Fig. 1B), and in only two instances did a mitral diastolic murmur persist. In these two patients the defect appeared on other grounds to be closed, and the murmur is attributed to mild congenital mitral stenosis; one of these was the patient with a single ventricle who also had a loud apical systolic murmur possibly due to mitral incompetence. Soft or moderate ejection systolic murmurs at the left sternal edge were quite common post-operatively and probably originated in the infundibulum or pulmonary artery; they were sometimes best heard near the apex. A basal diastolic murmur persisted in four. The second heart sound remained loud and closely split in Case 7, who still had substantial pulmonary hypertension after closure, but otherwise was usually softer and was sometimes widely split from right bundle-branch block.

The electrocardiogram in most cases showed a constant and unusual pattern. There was complete right bundle-branch block with the secondary R wave persisting as far as V5–V6 together with striking T-wave inversion in all chest leads. These appearances were presumably due to the intracardiac manœuvre and the ventriculotomy (Fig. 5).

Radiological assessment is probably not very profitable so soon after surgery, but in one case there was considerable diminution in heart size, and others have shown a definite reduction in pulmonary plethora.

Indicator dye-dilution curves performed on two patients post-operatively (Cases 5 and 6) have demonstrated the absence of a left-to-right shunt. Cardiac catherization is being deferred until a year or more after closure of the defect.

Conclusions

Our results harmonize with those of other workers in showing that closure of ventricular septal defects can be carried out in special centres as a routine surgical procedure with an acceptably low mortality in suitable cases. The indications and contraindications to operations have been outlined, but in assessing cases for operation we have experienced two main problems: first, the detection of additional lesions; and, second, in predicting whether a good haemodynamic response will result from closure.

The most important additional defect is a patent ductus, for it renders perfusion impossible. As already mentioned, this lesion was definitely diagnosed (by aortography) in only one of our four patients with it, though it was queried in one other. We suspect the diagnostic difficulty may lie in the fact that in patients with a V.S.D. the duct is virtually functionless and therefore gives rise to practically no direct signs. Support for this hypothesis is given by the absence of a thrill over the ductus at operation in three of the four patients and by the findings in Case 20. In this last patient, prior to aortography, 2 ml. of indicator dye was injected into the aorta via a retrograde arterial catheter, and no recirculation due to dye entering the pulmonary artery (Swan and Wood, 1957) was found. Further, at operation, no change in right heart or systemic pressure was noted when the duct was ligated. One patient (Case 21) was found at operation to have severe aortic incompetence, and clinically this was not diagnosed with certainty.

The other problem is that of predicting which patients will achieve a substantial fall in pulmonary artery pressure after closure. In this respect, other workers (Zimmerman *et al.*, 1957) have emphasized the importance of the actual level of the pulmonary artery pressure, but in our series this has not been helpful. We believe that the pressure must be considered in relation to pulmonary flow and that it is useful to calculate the pulmonary arteriolar resistance. However, the difficulty in young children of measuring the oxygen consumption, and also other factors, make the calculated resistance in many cases at best an approximation. It may turn out to be just as helpful to consider simply the oxygen saturation in the pulmonary artery, which has been over 80% in all our patients whose pulmonary pressure fell after closure. As mentioned earlier, it is necessary to consider all aspects in deciding for or against operation in the borderline cases with a high pulmonary resistance. No patient should be categorically denied operation if there is evidence of an appreciable left-to-right shunt, but when the pulmonary resistance is high and the unfavourable features already mentioned are present, a much higher operative mortality must be faced. It is clear from our results, however, that a number of patients who might in other centres be considered inoperable have had their defects successfully closed.

It must be emphasized that, in such a rapidly expanding field, views necessarily change fast as a result of new experience. Firm rules should not therefore be formulated until opinion has crystallized in the light of further knowledge of the problems involved.

Summary

Twenty-one patients with ventricular septal defect have been treated by open surgery using extracorporeal circulation.

The clinical features, indications for operation, surgical technique, and post-operative care are presented.

The results of surgical treatment are given and the implications of these are discussed.

We are indebted to Dr. R. E. Bonham-Carter, not only for referring many of these patients, but also for his continued encouragement and support; to Dr. J. D. James and Dr. P. B. Booth and the staff of the North London Blood Transfusion Service for their unfailing co-operation; to Professor J. V. Dacie and his colleagues in the department of haematology in the Postgraduate Medical School of London; and to the matron and nursing staff of Hammersmith Hospital. To Mr. J. R. Robson, Mr. E. Gains, Miss M. Murphy, and Mrs. E. Victor, the technical staff of the department of surgery, and to Mr. C. Lordon and the staff of the workshops of the Postgraduate Medical School we owe a special debt of gratitude.

Mr. Z. F. Kellerman and the staff of Messrs. New Electronic Products Ltd. have since 1950 given generously of their services and have unhesitatingly met the technical challenge.

To the Nuffield Foundation we are particularly indebted; they, by financial assistance, not only ensured the development of the apparatus but also its clinical success by their support to the project as a whole.

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Natural Causes, a new play on a challenging theme by Mrs. Vera Colebrook, was given a number of performances in London last month at the Hovenden Theatre Club. The action of the play takes place in the country house of an old lady who has just suffered a cerebral haemorrhage, complicated by the onset of pneumonia. Her family doctor had previously given her a solemn promise that should she fall seriously ill he will not administer any antibiotic or other drug that may prolong her life—or, rather, "prolong her death." On the insistence of her daughter-in-law, a well-known London consultant is called in: he advises injections of penicillin. The family doctor refuses to give these, telling the consultant of his promise and insisting that there is all the difference in the world between administering a lethal dose and withholding a life-saving drug. The old lady's two children want their mother to die as she had lived, with dignity and without fear of mental deterioration. But her shrewish daughter-in-law desires only that her mother-in-law's life might be prolonged for the sake of the benefits her annuity brings to the family. The Hovenden Players, directed by Miss Valery Hovenden, were completely successful in bringing out the realism of this situation. A philosophical nurse—who assumes a more pronounced Irish brogue with private cases, because "it goes down so lovely with the patients"—adds a touch of humour to the play, which is not concerned with "mercy killing" but rather with the truth or otherwise of Clough's "Thou shalt not kill, but needst not strive officiously to keep alive." The whole vexed problem, while remaining unsolved, is given an unexpected twist by the London consultant at the end of the play.

STAPHYLOCOCCAL INFECTION RESISTANT TO CHLORAMPHENICOL, ERYTHROMYCIN, AND NOVOBIOCIN

EFFECT OF ANTIBIOTIC COMBINATIONS ON THE EMERGENCE OF RESISTANT STRAINS

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Control of the use of antibiotics in hospital communities is imperative if we are to combat the adaptability of the staphylococcus to these agents. Until recently most hospitals in Great Britain have tried to keep erythromycin and novobiocin in reserve, to be used only for the treatment of staphylococcal infection resistant to all other antibiotics. By 1957, however, about 50% of all staphylococcal infection occurring in many hospitals was found to be resistant to penicillin, streptomycin, and tetracycline, so that erythromycin and novobiocin inevitably had to be used more extensively.

The danger of the increased use of these two drugs is obvious, since it is well recognized that staphylococci develop resistance to erythromycin and novobiocin more readily than to any other antibiotic except streptomycin (cf. Hobson, 1954; Garrod and Waterworth, 1956; Lin and Coriell, 1957). Moreover, this change occurs quite often during the treatment of staphylococcal infections with erythromycin (Thomson *et al.*, 1956) and novobiocin (Nichols and Finland, 1956), and the spread of erythromycin-resistant strains in a hospital where the use of this antibiotic is extensive may be very rapid (Lepper *et al.*, 1954).

In an attempt to combat this situation a policy for the control of antibiotics was introduced into this hospital at the beginning of April, 1958. The essential items of the policy were: firstly, abandonment of penicillin except in certain wards of the hospital, and, secondly, the use of two antibiotics in combination wherever possible and always when erythromycin or novobiocin was used.

About six months previously a cross-infection committee was appointed to investigate staphylococcal infection in the hospital and to introduce measures for its control. The effect of these measures and that of the antibiotic policy are inextricably confused. Nevertheless analysis of the antibiotic sensitivity pattern of all staphylococcal infections in the hospital throughout the year has brought to light certain facts about the emergence of erythromycin- and chloramphenicol-resistant strains which are considered worth reporting.

*In receipt of a grant from the Medical Research Council.

Bacteriological Methods

All staphylococcal infections in the wards of the hospital between October 1, 1957, and September 30, 1958, were studied bacteriologically. The period covered thus included six months before the introduction of the antibiotic policy and the first six months of its operation. The strains of *Staph. pyogenes* isolated were tested for sensitivity to penicillin, streptomycin, tetracycline, chloramphenicol, erythromycin, and novobiocin by the ditch-plate method. The concentration of antibiotics used in the ditch was: penicillin, 10 units per ml.; streptomycin, 50 or 200 g. per ml.; chloramphenicol, 50 g. per ml.; and tetracycline, erythromycin, and novobiocin 25 g. per ml. The Oxford staphylococcus was streaked across the centre of each plate as a control.

Strains were recorded as sensitive if they showed a degree of sensitivity similar to that of the Oxford staphylococcus, resistant if they grew up to or across the ditch, and partially resistant if there was an intermediate degree of inhibition. Representative strains were also tested by a serial dilution method in broth. The latter tests showed that strains recorded as partially resistant were often only two to four times less sensitive than the standard organism, but strains recorded as resistant always showed a more than eightfold difference.

Most of the strains on first isolation and those showing a change in sensitivity pattern were phage-typed by the method of Williams and Rippon (1952) using 21 phages.

Antibiotic Administration

After the introduction of the antibiotic policy in April, 1958, the use of drug combinations caused an increase in the consumption of most of the antistaphylococcal antibiotics except penicillin. The approximate changes were as follows: Penicillin, ÷ 3.2; tetracycline, × 1.4; chloramphenicol, × 1.6; erythromycin, × 2; novobiocin, × >5.

In the six months following the introduction of the antibiotic policy 284 patients were treated with chloramphenicol, 275 with erythromycin, and 170 with novobiocin. The most frequently used combinations were erythromycin and novobiocin (108 patients) and erythromycin and chloramphenicol (69 patients). Further details of the use of these three antibiotics are given in Table I. Similar figures are not available for the period before the antibiotic policy.

TABLE I.—*Number of Patients Treated with Chloramphenicol, Erythromycin, and Novobiocin, April 1-September 30, 1958*

	Total	In Combination with				Alone*
		Chlor.	Ery th.	Novo.	Other Antibs.	
Chloramphenicol	284	—	69	8	70	137
Erythromycin ..	275	69	—	108	45	53
Novobiocin ..	170	8	108	—	25	29

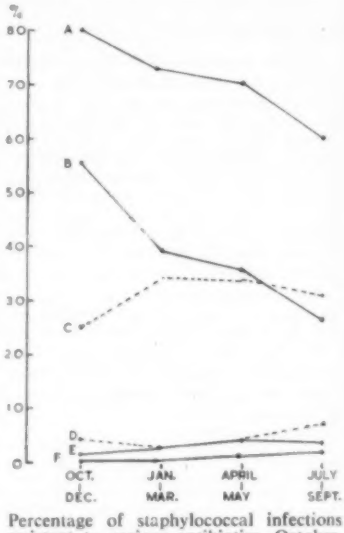
* Or in combination with a sulphonamide preparation.

Analysis of Sensitivity Patterns

A total of 982 staphylococcal infections were present in the hospital during the year. Antibiotic sensitivity has been analysed separately for each quarter, and the results are presented in the Chart. The total numbers of staphylococcal infections in each quarter were respectively 247, 245, 270, and 220.

It will be seen that the incidence of infection resistant to penicillin fell from 80% at the beginning of the year to 60% at the end. This is associated with a corresponding fall in the incidence of tetracycline-resistant infections (from 55% to 27%), practically all of which were also resistant to penicillin and which were in most instances the result of cross-infection in the hospital. The percentage of infections resistant to penicillin and sensitive to tetracycline rose slightly in the second quarter and thereafter remained steady.

In the first quarter of the year the incidence of staphylococcal infection resistant to penicillin and tetracycline was 46 per 1,000 admissions to the hospital. The cross-infection committee appointed at the beginning of the investigation recommended a number of measures for the control of cross-infection which were put into operation throughout the year. Probably as a result of these, although seasonal influences cannot be excluded, the corresponding figures for the remaining three quarters of the year were respectively 33, 32.7, and 20. The fall in the percentage of staphylococcal infections in the hospital that were resistant to penicillin and tetracycline is almost certainly a reflection of this. It is probably too early for the antibiotic policy introduced in the middle of the investigation to have had much effect on the incidence of penicillin-resistant infection.



Percentage of staphylococcal infections resistant to various antibiotics, October, 1957, to September 30, 1958. A=Penicillin. B=Tetracycline. C=Penicillin resistant and tetracycline sensitive. D=Erythromycin. E=Chloramphenicol. F=Novobiocin.

The percentage of infections resistant to chloramphenicol, erythromycin, and novobiocin remained low throughout the year. Since, however, nearly all these infections were also resistant to penicillin, streptomycin, and tetracycline, their importance cannot be exaggerated. The figures for erythromycin in each quarter were respectively 4.8, 2.8, 4.0, and 6.4, and the significance of the slight rise in the last quarter is increased by the accompanying fall in the incidence of multiple resistant infection as a whole.

Chloramphenicol-resistant Infection

The incidence and source of chloramphenicol-resistant infection are summarized in Table II. In the whole year there were 30 infections resistant to this antibiotic, and on

TABLE II.—*Chloramphenicol-resistant Infections*

	Total No. of Infections	No. of Strains of *Staph. pyogenes*	No. of Strains also Resistant to Erythromycin
Oct. 1 to March 31 ..	14	11	4
April 1 to Sept. 30 ..	16	12	4
	30	23	8
Source of Chloramphenicol-resistant Strains			
Isolated from patients on admission ..		3	1
Chloramphenicol-sensitive strain developed resistance to chloramphenicol during treatment with:			
Chloramphenicol and erythromycin		5	2
Erythromycin alone		1	1
First strain isolated from patients who had been treated with:			
Chloramphenicol alone or plus tetracycline		2	1
Chloramphenicol plus erythromycin		3	1
Erythromycin plus tetracycline ..		1	1
Other strains		8	1
		23	8

All strains were resistant to penicillin, streptomycin, and tetracycline except those isolated on admission. All strains were sensitive to novobiocin and vancomycin.

the basis of bacteriophage typing it was shown that the 30 infections were probably caused by 23 strains of *Staph. pyogenes*. Three of the strains showed partial resistance and 20 were recorded as resistant. It will be seen that there is no significant difference in the figures before and after introduction of the new antibiotic policy.

Of the 23 strains involved, three were isolated from patients on admission. The remaining 20 were all resistant to penicillin, streptomycin, and tetracycline, as well as to chloramphenicol, and seven, together with one strain isolated on admission, were also resistant to erythromycin. In six instances strains of the same phage-type were isolated on two occasions from the same patient, the first being chloramphenicol-sensitive and the second chloramphenicol-resistant, and three of these strains developed resistance to erythromycin at the same time. Five of the six patients from whom these strains were isolated had been treated with chloramphenicol and erythromycin, and one with erythromycin but not chloramphenicol.

In 14 cases the only staphylococcus isolated was chloramphenicol-resistant. Five of the patients from whom these strains were isolated had previously had chloramphenicol and one erythromycin. The remaining eight strains were isolated from patients who gave no history of recent antibiotic treatment.

Erythromycin-resistant Infection

Table III summarizes the information in relation to erythromycin-resistant infection. In the whole year 23 strains of *Staph. pyogenes* resistant to this antibiotic were responsible for 44 infections. In the first half of the year eight strains caused 19 infections, whereas in the first six

TABLE III.—*Erythromycin-resistant Infections*

	Total No. of Infections	No. of Strains of *Staph. pyogenes*	No. of Strains also Resistant to Chloramphenicol
Oct. 1 to Mar. 31 ..	19	8	4
April 1 to Sept. 30 ..	25	15	4
	44	23	8
Source of Erythromycin-resistant Strains			
Isolated from patients on admission ..		3	1
Erythromycin-sensitive strains developed resistance to erythromycin during treatment with:			
Erythromycin alone or plus tetracycline		3	1
Erythromycin plus chloramphenicol		4	2
First strain isolated from patients who had been treated with:			
Erythromycin alone or plus tetracycline		3	1
Erythromycin plus chloramphenicol		4	1
Chloramphenicol without erythromycin		3	1
Other strains		3	1
		23	8

All strains were resistant to penicillin, streptomycin, and tetracycline except those isolated on admission. All strains were sensitive to novobiocin and vancomycin.

months of the antibiotic policy 15 strains caused 25 infections. Two of the 23 erythromycin-resistant strains were recorded as partially resistant and 21 as resistant. It was noted, however, that many strains which were resistant on primary isolation became less resistant after subculture in the laboratory. Thirteen of the strains were tested against spiramycin: three were as sensitive as the Oxford staphylococcus, four showed a twofold, and six a fourfold increase in resistance to this antibiotic.

Three of the strains were present in patients on admission. The remaining 20 were all resistant to penicillin, streptomycin, and tetracycline, as well as to erythromycin, and eight were also resistant to chloramphenicol. In seven cases erythromycin-sensitive and erythromycin-resistant strains of the same phage-type were isolated consecutively from the same patient, and three of the strains showed a corresponding increase in resistance to chloramphenicol. All seven patients had been treated with erythromycin—four in combination with chloramphenicol and three alone or in combination with tetracycline, to which the initial strain was not sensitive.

In 13 instances the only strain of *Staph. pyogenes* isolated was erythromycin-resistant. Ten of the patients concerned had previously had antibiotic treatment: three with erythromycin alone or plus tetracycline; four with erythromycin and chloramphenicol; and three with chloramphenicol but not erythromycin. The remaining three strains were isolated from patients who had not had recent treatment with antibiotics.

TABLE IV.—*Novobiocin-resistant Infections*

	Total No. of Infections	No. of Strains of *Staph. pyogenes*
Oct. 1 to March 31	2	2
April 1 to Sept. 30	7	2
	9	4
Source of Novobiocin-resistant Strains		
Novobiocin-sensitive strain developed resistance to novobiocin during treatment with:		
Novobiocin alone		1
Novobiocin plus erythromycin		2
Other strains		1
		4

Three strains were resistant to penicillin, streptomycin, and tetracycline; and sensitive to chloramphenicol, erythromycin, and vancomycin. One strain was sensitive to penicillin, streptomycin, tetracycline, chloramphenicol, erythromycin, and vancomycin.

Novobiocin-resistant Infection

Throughout the year only four strains of *Staph. pyogenes* resistant to novobiocin were isolated (see Table IV), two in each half. Three of the strains were each isolated from only one infection. The fourth strain was responsible for infections in four children and two nurses in the same ward.

Three of the strains were also resistant to penicillin, streptomycin, and tetracycline, and sensitive to chloramphenicol, erythromycin, and vancomycin. One strain which developed resistance during novobiocin treatment was sensitive to all other antibiotics tested. The source of the strain which caused six infections is completely unknown. The remaining three strains all developed resistance during treatment with novobiocin, in two cases given in combination with erythromycin and in one case given alone.

Association of Chloramphenicol and Erythromycin Resistance

A number of observations in this study indicate an association between chloramphenicol and erythromycin resistance. Thus eight of the erythromycin-resistant strains were isolated from patients who had previously had erythromycin and chloramphenicol. In no instance, on the other hand, was an erythromycin-resistant staphylococcus isolated from a patient treated with erythromycin and novobiocin, in spite of the fact that after the introducion of the antibiotic policy 108 patients were treated with the latter combination and only 69 with erythromycin and chloramphenicol.

No fewer than 8 of the 23 erythromycin-resistant strains also showed resistance to chloramphenicol. In three cases strains of the same phage-type were isolated on two occasions from the same patient, the first being sensitive to both these antibiotics, and the second resistant. Two of the patients concerned had been treated with chloramphenicol and erythromycin, and one with erythromycin only. Three other strains showing this double resistance came from patients who had recently had antibiotic treatment, one with both the antibiotics concerned, one with erythromycin, and one with chloramphenicol.

With two strains, both of which were responsible for small outbreaks of infection (reported elsewhere; cf. Barber and Dutton, 1958), the resistance to chloramphenicol was inconstant. Thus strains resistant to penicillin, tetracycline, and erythromycin of a single phage-type infected several patients in one ward, and some of the cultures isolated were grossly resistant to chloramphenicol, whereas others were as sensitive as the Oxford staphylococcus. In one case the initial patient had been treated with erythromycin only, and in the other the patient had had a number of antibiotics, including chloramphenicol, but had never had erythromycin.

It seems probable from these observations that there is some cross-resistance between erythromycin and chloramphenicol, and preliminary studies *in vitro* have shown this to be the case. The investigation will be published in full elsewhere (Csillag and Barber), but it has already been found that strains of *Staph. pyogenes* rendered resistant to erythromycin by passage in this antibiotic develop a moderate and sometimes transitory increase in resistance to chloramphenicol.

Discussion

This investigation emphasizes the danger of erythromycin-resistant infection becoming a hospital problem if the unrestricted use of erythromycin is permitted. Since there is evidence of cross-resistance between erythromycin and chloramphenicol, combined treatment with these two antibiotics offers no solution. Monnier and Schoenbach (1951) and Fusillo, Romansky, and Kuhns (1953) demonstrated a similar increase in resistance to chloramphenicol when staphylococci were passaged in the presence of tetracycline compounds. A study of cross-resistance with chloramphenicol and other antibiotics is now in progress.

Combined treatment with erythromycin and novobiocin seems more promising. Lowbury (1957) showed that the combination of these two antibiotics delayed the emergence of erythromycin-resistant staphylococci *in vitro* and *in vivo*. In the investigation here recorded no erythromycin-resistant staphylococci were isolated from 108 patients treated in this way. This number is, of course, small, and it is too early to say whether this combination will do more than postpone the evil day; but even this is of value, since it might tide us over until new antibiotics were available.

Scott and Waterworth (1958) treated 110 patients suffering from boils with a seven-day course of erythromycin (55 patients) or E 129 (55 patients) and found no instance of increased bacterial resistance to either antibiotic. Coagulase-positive staphylococci were, however, isolated from only 15 of the original boils after treatment, although a further 23 strains, which were isolated from fresh lesions developing during or after treatment, were also found to be erythromycin-sensitive.

The *British Medical Journal* (1958) asked whether the determining factor in the development of resistance to erythromycin was "the nature of the lesion, dosage, or duration of treatment, or a property of the staphylococcus itself." In the present series length of treatment was not necessarily prolonged, and some of the patients had been treated with erythromycin for only a few days before the appearance of erythromycin-resistant staphylococci. With regard to the lesions, however, although one strain came from a boil treated with erythromycin alone, most of the strains came from more severe infections such as pneumonia, lung abscess, peritonitis, or post-operative sepsis.

The type of staphylococcus concerned is probably of considerable importance. In the present series nearly all the strains showed multiple resistance to antibiotics, and it has been suggested that such strains may be highly mutagenic (Treffers *et al.*, 1954; Barber and Dutton, 1958). All the erythromycin-resistant strains were also shown to belong to phage groups III except for a few strains of type 80. It has been shown that group III staphylococci yield antibiotic-resistant variants more readily than do other strains (Barber and Whitehead, 1949; Rountree and Thomson, 1949; Barbour and Edwards, 1953), and the same may well be true of phage-type 80 staphylococci, which have recently become a hospital menace (Rountree and Freeman, 1955; Anderson and Williams, 1956; Gillespie and Alder, 1957; Duthie, 1957).

While staphylococci of such virulence and adaptability continue to circulate in hospital communities it is important that the use of erythromycin should remain under strict control. Although novobiocin, vancomycin, ristocetin, and kanamycin have been added to our antistaphylococcal armoury, the last three have serious toxic effects, particularly on the eighth nerve. Since novobiocin, like erythromycin, has the defect that staphylococci readily become resistant to it, both should be used sparingly, and neither except in combination with each other or another chemotherapeutic agent.

Summary

A policy whereby antistaphylococcal antibiotics were used only in combination was introduced into a large general hospital.

The antibiotic sensitivity of all strains of *Staph. pyogenes* isolated from infections in the hospital was studied during a period lasting six months before the introduction of this policy and six months afterwards.

Analysis of erythromycin- and chloramphenicol-resistant infection has shown evidence of cross-resistance between these two antibiotics. Of 23 erythromycin-resistant strains, 11 came from patients who had been treated with chloramphenicol (in eight cases in combination with erythromycin and in three cases without). Moreover, eight of the erythromycin-resistant strains also showed resistance to chloramphenicol, although in two cases the patient had been treated with erythromycin but not chloramphenicol.

No such cross-resistance was noted between erythromycin and novobiocin, and of 108 patients treated with this combination none yielded a staphylococcus resistant to erythromycin, although in two instances strains resistant to novobiocin were isolated.

It is a pleasure to thank the many clinical colleagues who co-operated in this investigation and, in particular, Dr. Peter Elmes, without whose energy and enthusiasm the work would not have been possible. Our thanks are also due to Eli Lilly and Company for free supplies of erythromycin ("ilotycin").

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NEPHRITIS IN NORTH YORKSHIRE

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Outbreaks of acute glomerulonephritis have been reported, associated in recent years with *Streptococcus pyogenes* type 12 and sometimes with other types (Rammelkamp, 1954). As the potentially epidemic nature of nephritis may still not be generally recognized, some events in northern Yorkshire during the past 18 months are recorded.

Present Investigation

On March 25, 1957, it was learnt that during the last fortnight in January there had been 24 cases of acute pharyngitis among 56 boys in a residential school for the educationally subnormal, followed 10–19 days later by acute nephritis in four of them and suspected rheumatic fever in a fifth. On February 15 all the children were given oral penicillin, and this was continued for three days. The school, which was situated in a small and rather isolated village, was visited on March 26, and nose and throat swabs and urine specimens were obtained from the 24 children who had been ill. *Str. pyogenes* type 12 was isolated from seven; the urine of three of the four who had had nephritis still contained blood cells in moderate numbers, and that of the fourth was clear; red cells were also present in the urine of five other children, two of these specimens also showing casts.

In order to ascertain the extent and effect in the community of the type 12 infection, the small local primary school (school A), a quarter of a mile (400 m.) away, was visited on March 31 and specimens were obtained from the pupils. It was clear from the results (see Table), and from the fact that a clinical case of nephritis was found, that the outbreak was not limited to the residential school. Six primary schools in villages within a 5-mile (8-km.) radius were therefore visited during the next few days, and evidence of type 12 infection was found in three of them (B, C, and D). The Table shows that 11 streptococcal strains isolated from school C were of a degraded type. Dr. R. E. O. Williams, of the Streptococcal Reference Laboratory, who was responsible for the typing of all the strains mentioned in this report, found that these strains belonged to a type related to 12, but he could not be certain whether they were derived from type 12 strains. The strains isolated from the other schools were typed without difficulty. Urine was obtained from the children in the four positive schools (A, B, C, and D), and in one negative school (E). Red blood cells were seen in 31 of the 146 specimens from the positive schools but not in 18 specimens from the negative school. Only one of these children had symptoms of nephritis—the case in school A already mentioned.

Incidence of Str. pyogenes Type 12, Acute Nephritis, and Symptomless Urine Abnormalities in Pupils Attending Certain Schools in March–April, 1957

School	No. of Pupils				
	Examined	Harbouring *Str. pyogenes* Type 12	With Acute Nephritis	Showing Symptomless Urine Abnormalities	
				Red Blood Cells	Casts
Residential ..	24	7 (29%)	4	5	2
A*	26	14 (54%)	1	11	4
B	34	16 (47%)	0	6	0
C	48	11 (23%) (degraded)	0	13	2
D	38	3 (8%)	0	0	0
E	18	0 (—)	0	0	0
Secondary	570	32 (6%)	0	Not tested	
Secondary Form 1B	32	9 (28%)	0	3	0

* In the same village as the residential school.

Children over the age of 11 years from the affected villages attended a large bilateral secondary school 7 miles (11 km.) away from the centre of the original outbreak. In order to assess the extent to which infection had been carried into an unaffected locality by the older children, it was decided to investigate children at this school. Throat and nose swabs were taken from the whole school early in April and urine specimens were examined from children in the form (1B) showing the highest proportion of type 12 strains. The number of red cells found in the urinary deposits of children from the different schools ranged from 1 to 50 per high-power field; as there was no standard of normality with which to compare these findings, urine samples were obtained from 287 children of similar age in two schools 20 miles (32 km.) away from the affected area. No red cells or casts were found in any of them.

No further cases of nephritis came to our notice until December, 1957, when three occurred in the Northallerton District, some 25 miles (40 km.) north of the original outbreak. Further cases occurred in the York City and Northallerton areas during January and February, 1958, so at the beginning of March circular letters from the county medical officer and from the pathologist in York were sent to all doctors in York and the North Riding warning them of the situation and asking for information on cases of nephritis. During the first six months of 1958, 27 cases were unofficially notified in and around York City, and a further 18 in or near Northallerton. In York, 25 of the 27 cases were admitted to hospital and two were treated at home. Four of the hospital cases were admitted to surgical wards—three adults for investigation of haematuria and one child as an abdominal emergency. All 27 patients were examined bacteriologically, but mostly some time after onset and many had already received antibiotic treatment; *Str. pyogenes* type 12 was isolated from nine cases and type 22 from another. In Northallerton, 15 of the 21 cases were admitted to hospital and six treated at home. Throat swabs were taken from 14 cases; eight yielded *Str. pyogenes* type 12 and one a group B streptococcus. One patient, although having a negative swab, had antibodies to *Str. pyogenes* type 12 in her blood, and another, also with a negative swab, had a sibling from whom a type 12 strain was isolated.

We are thus aware of 53 cases of frank acute nephritis in York or the North Riding during the past two winters—5 in the first winter and 48 in the second. *Str. pyogenes* type 12 was isolated from 19 of them, and many of the remainder were either not swabbed or not swabbed at a suitable time. In addition, 38 children in schools were found to have red cells in the urine but no symptoms of nephritis; *Str. pyogenes* type 12, or a related type, was isolated from 19 of these. All but four of the cases of nephritis had a history of sore throat or otitis media, and so did most of those with haematuria but no clinical illness. In some cases, however, the initial infection was not severe enough for the patient to seek medical advice. No cases followed scarlet fever.

There was no evidence that the infection was transmitted except by direct contact. The sexes were equally affected, and the commonest age group was 5–15 years, which was the group most fully investigated. Nevertheless adult cases of nephritis occurred in both sexes, the oldest being a woman of 37 and a man of 44. The average period between infection and the onset of nephritis in those giving a reliable history was 14 days; the time ranged from 7 to 24 days, but in only two cases did it exceed 18 days.

Summary

An epidemic of nephritis associated with *Streptococcus pyogenes* type 12 occurred in York and in predominantly rural areas of the North Riding during the winter months of 1957 and 1958. In several schools in which there was evidence of type 12 infection in 1957 some children were also found with symptomless haematuria. Spread of infection took place in schools and at home. Symptoms of the initial streptococcal infection were usually present but often slight, and were followed by the onset of nephritis 7 to 24 days later.

We are indebted to Dr. R. E. O. Williams for typing the strains; to Dr. H. Gray, M.O.H. Easingwold R.D., Dr. J. L. Cotton, M.O.H. Northallerton U. and R.D., and Dr. A. K. Thomas, of Tollerton, for their co-operation and help in the investigation; to Dr. J. A. Fraser, C.M.O.H. North Riding of Yorkshire, for his advice on many points; and to all those practitioners who went to the trouble of reporting cases and contacts.

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AN OUTBREAK OF NEPHRITIS IN NORTHAMPTONSHIRE

BY

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In April, 1957, the head teacher of a village school telephoned the county health department to say that three children in the upper junior class at his school had fallen ill with nephritis within a period of a month. A fourth child, in the lower junior class, had been taken by his parents to Portsmouth, where he had become ill; the doctor had diagnosed pyelitis and sent the family home. Another child in the village attending a different school was under observation by the family practitioner with a sore throat and puffiness under the eyes. As a result of this outbreak there was considerable anxiety amongst the parents in the village; some of the children were being kept away from school unnecessarily, others were returning to school in an unfit condition. Although there had been a considerable amount of upper respiratory infection in the infant and lower junior classes in the early months of the year, it was not until April that the upper junior class had been affected, and it was in this month that nephritis had suddenly arisen as a complication.

Investigation

The school, which was visited on the same day, was soundly constructed and the rooms were well ventilated and not overcrowded. All the children and staff were examined, and swabs were taken from any lesions suggestive of streptococcal infection. Group A type 12 haemolytic streptococci were obtained from lesions in two children in the upper junior class in which the cases of nephritis had occurred. One of the two children had a sore throat, the other a sore place in the nostril. The desks occupied by these two children and the children with nephritis were not grouped, but were dispersed among other desks in the classroom.

Apart from reassurance and advice to the head teacher it seemed desirable to assess the size of the outbreak. From discussions with practitioners it was evident that other cases had occurred in near-by villages, and from the paediatric department it was learned that about 25 children from the county had been admitted to hospital with nephritis since the previous October. In order to obtain further information Dr. C. M. Smith, the County Medical Officer of Health, wrote to all doctors practising in the county giving them particulars of the outbreak and asking to be notified of any cases under their care. From the replies received it is possible to present the following information.

Epidemiological Distribution

Only four cases were ascertained in 1955 (Fig. 1). Then in the first quarter of 1956 five children living in Kettering were taken ill; three of them lived in the same neighbourhood—two in houses almost opposite each other. Two months later cases were reported from Wellingborough, where the infection continued until June of the following year. By March and April, 1957, the infection had spread south-west to Northampton County Borough and had reached considerable proportions, the incidence in the county town being reflected in several small outbreaks in the outlying village communities, such as that already described. The infection then appeared to continue south-west, and by the late autumn it looked as though it was dying out. Over the winter months, however, another, and smaller, outbreak occurred, which was centred round Northampton, and again cases occurred in outlying villages and towns which had not been affected in the first outbreak.

It would be unwise to draw conclusions from data which are probably incomplete. Nevertheless, from the cases ascertained it can be said that there was no similarity between the distribution of cases of scarlet fever and nephritis during the period under review. Many of the scarlet-fever notifications were sporadic "dropping" cases, so that inevitably there were occasions when both conditions occurred in the same area at the same time. Beyond this, however, there was no evidence of association in the spread of the two infections.

Age and Sex Incidence.—In all, 89 cases were ascertained. Seventy-three occurred in children, 52% of whom were boys. One child under 3 was affected; 12 cases occurred in children aged 3 and 4 years; 45 cases in children aged 5 to 9 years; 15 cases in children aged 10 to 15 years (Fig. 2); and 16 cases in persons over 15 years.

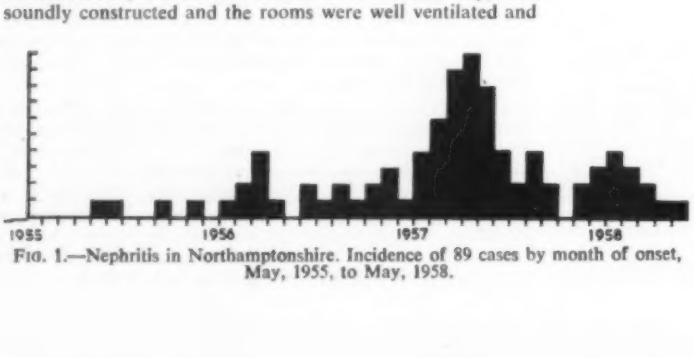

FIG. 1.—Nephritis in Northamptonshire. Incidence of 89 cases by month of onset, May, 1955, to May, 1958.

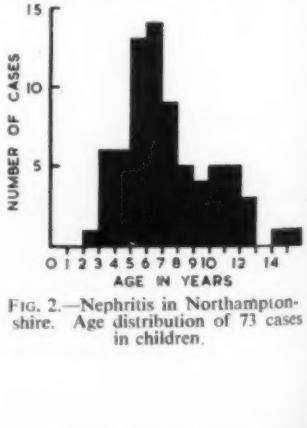

FIG. 2.—Nephritis in Northamptonshire. Age distribution of 73 cases in children.

Clinical Picture

Most of the patients were children and were admitted initially to hospital. Parents gave a history of febrile illness two weeks previously, invariably with a sore throat or other obvious upper respiratory infection. Frequently oral penicillin had been given by the general practitioner. There then followed a period of apparent recovery until perhaps the day before admission, when the child again became unwell, with loss of appetite, lassitude, pallor and puffiness of the face, and, on occasion, headache. In some cases the parents had observed the passing of dark urine. On examination the urine was found to be loaded with albumin and gave a positive chemical test for blood, which was confirmed by microscopy.

Two weeks after the initial infection positive nose or throat swabs were obtained in a high percentage of children; in all others the anti-streptolysin titre was raised. The organism found was invariably the haemolytic streptococcus (Lancefield group A type 12). Approximately 60% had raised blood pressures, and in two cases this was high enough to produce hypertensive encephalopathy. One of these patients presented in the casualty department as a case of sudden blindness.

On admission to hospital the lingering presence of the streptococcus was always assumed and every patient received a 14-day course of intramuscular penicillin. Cases of hypertension were sedated and every patient was confined strictly to bed until the Addis count (a measure of microscopic haematuria) approached normal. When the number of red blood cells in an overnight 12-hour specimen of urine was down to 1,000,000, gradual mobilization of the patient began. He was allowed home when the red cells were less than 500,000. The average length of bed rest required was 15 weeks, though some cases took as long as 20 weeks to produce a normal Addis count. Hypertension rapidly disappeared, usually within 10 days. Several cases had grossly enlarged, pitted, and unhealthy tonsils, and one child had an infected aural polyp. These cases showed slow response to medical treatment, but when surgery was carried out the subsequent improvement was impressive.

After discharge from hospital all cases were followed up. Earlier cases showed an increase in the Addis count associated with comparatively mild upper respiratory infections. Many showed increased counts even without obvious infection. Later patients were sent home on small prophylactic doses of phenoxymethylpenicillin daily, and these have so far shown a remarkable improvement in the follow-up condition. It is too early yet to assess the long-term effects of the disease and the treatment, but from preliminary observations it would seem that there is unlikely to be any gross permanent renal damage.

Discussion

In the present outbreak the exchange of information between the health department and medical practitioners was probably of value. The experience obtained suggests that in future outbreaks of serious infections which are not notifiable it would be a useful measure to alert all practitioners as soon as possible, since early treatment may help in modifying the severity of the attack or preventing complications.

In view of the complications likely to arise from streptococcal reinfection, it is worth while considering whether schoolchildren should not receive special supervision after an attack of nephritis. Teachers could be advised that they should report at once to the principal school medical officer in the event of upper respiratory or cutaneous infections in the class or school. Any child at special risk of nephritis reinfection could then be temporarily excluded. It would seem advisable also that parents should be cautioned of the liability of reinfection, so that crowded gatherings were avoided until the child's resistance was considered satisfactory.

Summary

A description is given of an outbreak of nephritis in Northamptonshire due to group A type 12 haemolytic streptococci. In all, 89 cases were ascertained; 73 occurred in children under 16 years of age, 52% of whom were boys.

Many of the cases were notified by practitioners in response to a circular letter which notified them of the outbreak and asked for particulars regarding cases in their practice. Early exchange of such information would appear to be a useful measure in serious infections that are not notifiable.

No association was noted between the distribution of nephritis and scarlet-fever cases during the period under review.

The cases showed the familiar pattern of acute nephritis, though the severity varied greatly from patient to patient. Albuminuria and transient "frank haematuria" were constant features. Following initial penicillin (intramuscular), prolonged bed rest was the most important part of the treatment, its duration being dictated by weekly microscopy of the urine and E.S.R. estimation.

The importance of keeping post-nephritics free of further streptococcal infection is emphasized. In this respect the oral administration of phenoxymethylpenicillin is a safe and efficient method of prophylaxis. In addition it may be considered desirable to advise parents regarding the risk of reinfection, and for the children to receive special supervision at school.

We thank Dr. C. M. Smith, County Medical Officer of Health for Northamptonshire, for his advice; Dr. I. H. Gosset, consultant paediatrician, for permission to refer to cases under his care; and all medical practitioners in the county, without whose co-operation the outbreak could not have been investigated.

POSSIBLE DISADVANTAGES OF A CHEST RADIOGRAPHY SERVICE FOR GENERAL PRACTITIONERS

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It is common practice in many chest clinics to provide, in addition to normal consultations, special sessions to which practitioners may refer their patients for chest radiography only. These patients form a selected group in that they are usually referred because of symptoms which could arise from respiratory disease. If a chest radiograph shows an abnormality it is mutually understood by practitioner and physician that the patient may be recalled to the clinic for further investigation.

The diagnostic value of this service is demonstrated by the regularly high yield of abnormalities; its possible disadvantages are seldom even discussed. Disease not obvious on the chest film might be found by clinical examination. Moreover, a normal *x*-ray report from the clinic might allay practitioners' fears and, by false reassurance, delay diagnosis.

The following experiment was designed to determine, *in those patients whose chest radiographs were reported as normal*, (*a*) the amount of clinically discoverable disease present on attendance, (*b*) the incidence of early disease missed on radiography as represented by its appearance within the next few months, and (*c*) the extent to which normal *x*-ray reports influenced practitioners in their appreciation of any subsequent development.

Method

The routine "*x*-ray only" service in this clinic has always been conducted on 70-mm. roll film. Both postero-anterior and antero-posterior lordotic films are taken, and subsequently read by two observers independently to minimize error due to observer variation (Stradling and Johnston, 1955). In addition, during the period October, 1956, to May, 1957, inclusive, with the full co-operation of the practitioners concerned, certain of the referred patients underwent clinical examination at the time of routine radiography. To avoid bias and to obtain a group of suitable size for analysis, a systematic sampling method was employed; all patients born in the month of May were invited to co-operate, and none refused to be examined.

At the clinical interview the physician took a careful history, conducted a full physical examination, including urinalysis, and viewed a full-sized chest radiograph. When necessary, patients were referred to other hospital departments for investigation. When the 70-mm. films were read on the following day the patients' names on these films were obscured to avoid possible recognition before the observers had given their reports. If an abnormality was found during this routine film reading the patient was excluded from further study in the systematic sample even if already examined clinically. Thus further consideration is of a representative group of patients whose miniature radiographs were all considered normal.

During the same months a second systematic sample of patients (all those born in November) was collected for later analysis. These patients were not examined in the clinic, but those who were reported to have normal miniature radiographs were followed up four to eight months later by means of a questionary addressed to their practitioners. Inquiries were made to determine subsequent clinical developments within the follow-up period, any further action practitioners may have taken following the report of a normal chest radiograph, and in particular whether this report had led to diagnostic delay through the false reassurance of doctor or patient. It was specifically asked whether the report had been (*a*) of assistance, (*b*) of no help, or (*c*) actually misleading in this respect.

Results

Of 673 patients radiographed during the period under review, 155 (23%) were recalled for further investigation by the routine procedure when the miniature films were read. This again confirms the positive value of such a service and also establishes that the yield of abnormalities was in no way unusual during this period, for in 1955 and 1956 respectively 25% and 18% of the films proved to be abnormal. That the service itself provides representative material for analysis is shown by the figure of 4,000–5,000 miniature radiographs taken annually and the large number of practitioners referring patients.

The 74 patients forming the first systematic sample also proved representative in this respect, for 18 (24%) would have been recalled on viewing the 70-mm. films also. As members of the sample, however, they had already been examined and appropriate action taken. On no occasion was an abnormality discovered by the routine reading of miniature films in a patient already considered normal at the full examination undertaken as part of the experiment. Furthermore, no abnormality was discovered on the large radiographs that was not seen on the miniatures.

There remain in the first sample 56 patients whose miniature films were reported as normal. On physical examination 4 (5.4% of the sample) additional thoracic abnormalities were found in these patients. Two of these conditions (2.7%) proved significant and required treatment: one elderly man suffered from chronic bronchitis aggravated by excessive smoking, which he was advised to stop; another had an acute exacerbation of his chronic bronchitis, which was successfully treated with tetracycline. Relatively insignificant abnormalities not requiring treatment were found in the other two patients: one had mild costochondritis and the other a slight degree of pectus excavatum.

Significant extrathoracic disease was discovered in five patients (6.7%). One young woman had chronic paranasal sinusitis not previously diagnosed, two had iron-deficiency anaemia, and one had severe hypertension requiring hypotensive therapy. The fifth patient had cardiac neurosis: reassurance following full physical examination and investigation with normal findings led to relief of her symptoms. In two other patients (2.7%) insignificant abnormalities were discovered: mild systemic hypertension at the age of 77 and splenomegaly due to chronic malaria, already known to the practitioner.

By chance the second systematic sample also consisted of 74 patients. The number of abnormal reports on the miniature radiographs was 11 (13.5%), and these are not considered further. Questionaries were circulated in respect of the remaining 63 patients, whose miniature films were reported normal, and every one of the 32 practitioners involved responded to the inquiry. Only two patients are untraced: they failed to revisit their doctors and had apparently left the district.

There remain for analysis 61 replies relating to patients with normal radiographs. All these patients were seen by their doctors soon after the initial radiography, and of the 61 replies, 60 stated that the report had been of assistance in making a diagnosis; usually by narrowing the field of possibilities or practically excluding a more serious pulmonary disease such as carcinoma or tuberculosis. Of these 60 patients, their practitioners had considered 48 normal or to have recovered from the illness which prompted reference for chest radiography. In the other 12 (16.2% of the sample) definite diagnoses were made by the practitioners: bronchitis with or without asthma was present in eight patients (10.8% of the sample) and non-thoracic disease in four others (5.4%). The diagnoses were hepatitis, hypochromic anaemia, alcoholic dyspepsia, and gout.

The subsequent clinical status of all 61 patients was either known or checked on receipt of the replies. None had developed any further disease during the follow-up period. In one, however, carcinoma of the bronchus was diagnosed soon after follow-up was complete. This case is discussed below.

On only one occasion did a practitioner feel that the radiograph had not helped towards a diagnosis. This patient, with pain in the chest and chronic bronchitis, was considered to have two fractured ribs on subsequent clinical examination at another hospital. The fractures, notoriously difficult to diagnose radiologically, were not visible on rescrutiny of our films.

Discussion and Conclusions

Chest radiography services, similar to that described, are now provided for practitioners by a large proportion of chest clinics. The widespread acceptance of such a facility is largely based upon the undoubted convenience to both patient and practitioner and an appreciation by the majority of the profession of its intrinsic value as a diagnostic aid. Moreover, the public health value of these services is very real in the case of tuberculosis: it is usual to obtain a yield of cases approximately 10 times that from mass radiography surveys of presumably healthy populations

(Toussaint and Pritchard, 1944; Sutherland, 1952; Trenchard and Grenville-Mathers, 1952). Early diagnosis, so often achieved when radiology is applied promptly to patients with minor symptoms, helps to prevent further spread of his disease both in the patient and in the community. It is the general practitioner who is most often presented with the diagnostic opportunity. He must act, but can do so only if he has ready access to diagnostic radiology (Stradling, 1948).

Nevertheless, there has always been an uneasy feeling in the minds of some physicians that perhaps such services were misconceived. It is thought by them that the ready availability of chest radiography might encourage slipshod physical examinations; that the *x*-ray examination might be used as an unwise short-cut to diagnosis or as a method of passing to a colleague responsibility for further action. From this it is argued that diagnostic errors can be avoided only by full physical examination at hospital or clinic whenever patients attend for chest radiography. But this would defeat one of the main aims of routine radiography services—the ability to deal rapidly with as many patients as practitioners choose to refer. Certainly it is only by the use of radiography that patients with minimal or no symptoms will have their pulmonary disease discovered in an early and treatable stage. The fact that the examination is over quickly is one of the main attractions to the patient: many of these relatively fit people would not attend if they thought that a long interview and an examination were involved.

The advantages of such radiography services have long been accepted by most chest physicians as outweighing possible disadvantages. Indirect evidence that this is justified, based on a retrospective survey of radiographs taken at routine consultations in a chest clinic, has been provided by Bradbury *et al.* (1951). In a group of 200 consecutive new patients every one of the 21 shown to have abnormalities on full clinical examination was picked out for recall on resurvey of the radiographs alone.

Our direct assessment of the situation has confirmed our confidence in the radiography service provided. Only 2.7% of the first sample of patients investigated proved to have thoracic disease needing treatment at the time their miniature films were reported normal. The corresponding figure for non-thoracic disease was 6.7%. These abnormalities were all either known to the practitioners concerned or discoverable by clinical examination in the surgery.

Furthermore, it is significant that the figures for non-thoracic disease discovered by physical examination, either under conditions of controlled trial at hospital or in the practitioners' surgeries, proved similar (6.7% and 5.4%). This very similarity indicates to us that practitioners are not apparently being distracted from diagnosing extra-thoracic disease by the report of a "normal" chest radiograph. Far from suggesting that such a report delayed diagnosis, our findings have revealed it as a positive, welcome, and correctly used diagnostic aid. Of the 32 doctors circulated with the questionary, 16 added unsolicited footnotes indicating the great importance they attached to a freely available chest radiography service. None of the 61 patients with normal reports on their initial radiographs developed any significant illness during the follow-up period of four to eight months. It is felt that this period is long enough to have revealed any such illness that might have been present at a detectable stage when radiography took place. The bronchial carcinoma diagnosed in one patient soon after follow-up was completed is considered to be an unrelated finding. This patient was admitted urgently with superior vena caval obstruction ten months after the symptoms leading to radiography had subsided. It is unlikely that an earlier diagnosis would have been made had the original radiographs never been taken: the terminal symptoms had been present for only a few weeks.

The success of a freely available chest radiography service depends upon the mutual co-operation of general practitioner and chest physician. Each has his full part to play: the practitioner in referring any patient with even minor pulmonary symptoms; the physician in detecting the abnormal films and taking appropriate action on these. The practitioner also retains responsibility for those patients reported to have normal films: symptoms must be accounted for and further investigations arranged if this proves difficult. Radiography must be recognized for what it is—a diagnostic *aid* that must take its place with all others necessary for building up the full clinical picture. Repeat radiography at a suitable interval is essential if suspicious symptoms persist.

In our experience the necessary co-operation is fully obtainable. The high yield of initial abnormalities, the low yield of disease on additional physical examination, and the absence of serious developments during a period of follow-up, all indicate that such services are being used to the best advantage and that they are of the highest clinical and public health value. Disadvantages are more hypothetical than real, and are far outweighed by the advantages to practitioner, physician, and community alike.

Summary

Many chest clinics provide a chest radiography service for general practitioners in addition to the usual consulting sessions. The positive value of such a service is acknowledged, but its possible disadvantages have not previously been investigated.

Clinical examinations were made of 74 patients, chosen by a systematic sampling method from a group referred for "*x*-ray only." The thoracic abnormalities so discovered in those with normal chest radiographs represented 5.4% of the sample. Another 6.7% had non-thoracic diseases detected by clinical but not by radiological examination.

A second systematic sample was followed up some months later by a questionary addressed to the patients' practitioners. This showed that a similar incidence of thoracic and non-thoracic disease had been found by them. It is concluded that practitioners are not distracted from diagnosis by a report of a normal radiograph: such a report often proved of great value in excluding serious disease. The possible disadvantages of a chest radiography service for general practitioners are largely theoretical and are not borne out by practical experience.

We gratefully acknowledge constructive criticism from Drs. J. G. Scadding and Ian Sutherland. Our sincere thanks are also due to the many general practitioners who co-operated so fully and made the survey possible.

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The Ministry of Pensions and National Insurance has again published a *Digest of Statistics Analysing Certificates of Incapacity*. The new volume refers to the year 1955–6, but includes some comparison with previous years. The statistics do not cover illnesses which are too short for a claim to be made or sickness among people not eligible to claim. The *Digest* is available to interested persons on application to the Statistics Division of the Ministry at 10, John Adam Street, London, W.C.2.

GOLDBERG-MAXWELL SYNDROME

REPORT OF THE ANOMALY IN THREE SISTERS

BY

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In 1948 Goldberg and Maxwell described a case of feminine type of male pseudohermaphroditism and collected seven other cases from the literature which they believed belonged to the same group. Up till 1954, altogether 22 examples of Goldberg-Maxwell syndrome have been reported in the literature. Below is the report of this condition occurring in three sisters.

Case Report

A female Hindu, 21 years of age, married, was admitted at the A.H.M. and Dufferin Hospital, Kanpur, for the investigation and treatment of primary amenorrhoea. She looked perfectly feminine. Her height was 5 ft. 5in. (1.65 m.), chest 35 in. (0.89 m.), and waist 28 in. (0.71 m.). Her breasts were well developed and the areolae and nipples normal. Axillary and pubic hair were absent. On vaginal examination the external genitalia were found to be normal. The labia were shaped normally, the urethra was situated correctly, and the clitoris was of usual size. The vagina was of ordinary dimensions, being 3½ in. (8.9 cm.) in length and quite capacious. The vagina ended in a blind pouch and no cervix was felt or seen, the vaginal vault being a smooth dome with no elevation or depression. Nothing could be felt at the site of the uterus.

The patient had been married two years and was perfectly happy as the female partner. Her sexual inclinations were female and her libido was normal. Her family history was most interesting, as two of her sisters also showed the same abnormality. Her eldest sister, 25 years old, had been married for seven years, but had no children and had never menstruated. Unfortunately a physical examination could not be carried out on her as she was in Calcutta; but from the description given by her sister it was quite obvious that she also suffered from the same anomaly. The second sister was 23 years old, and had been a widow for five years. She had never menstruated and had no issue. Her appearance was feminine and she had well-developed breasts, but axillary and pubic hair was absent. The external genitalia and vagina were normal; the latter ended in a cul-de-sac, and the uterus and cervix were absent. The third, and youngest, sister was 12 years old, unmarried, and had small, adolescent breasts. The axillary and pubic hair had just started to appear and she had menstruated twice. External genitalia were normal. Rectal and vaginal examination could not be done. Skin specimens were taken for biopsy from the second and third sisters, but report on the nuclear sex could not be given as the preservation of tissue was not satisfactory.

Tests for the estimation of hormone levels in blood and urine could not be carried out owing to lack of facilities for hormone assay. Laparotomy was performed on July 25, 1957. The findings were as follows. The uterus was absent, and in its place there was a tiny nodule of fibro-fatty tisue. The tube, gonad, broad ligament, and round ligament were absent on the right side. On the left side the tube was absent; the broad ligament was very rudimentary, ending outwards in a thin crescentic fold. The left gonad was situated in the region of the left iliac fossa, attached by a fold of peritoneum to the posterior abdominal wall. It was about 3 in. (7.6 cm.) long and 1¼ in. (3.8 cm.) wide, and consisted of cysts 2 mm. to 1 cm. in diameter. A large piece was taken from the left gonad as a biopsy specimen, and the abdomen was closed.

The histological report on the specimen was: "Section shows number of tubular structures separated by a variable amount of fibro-collagenous stroma. These tubules are lined by one or two layers of rounded cubical cells. The cytoplasm of some of these cells is vacuolated or clear in appearance. The stroma in between these tubules contains small islands of Leydig cells. The latter are rounded or ovoid in shape, having intensely eosinophilic cytoplasm."

Discussion

Although only 22 cases of Goldberg-Maxwell syndrome have been described in the literature from 1948 to 1954, the condition is not so uncommon. In the last 10 months, while working in this hospital, besides the above-mentioned cases of three sisters, I have found this condition also in another patient, who complained of primary amenorrhoea and sterility. A skin biopsy specimen was taken for nuclear sexing, but she did not report back. I think many of these cases are sent away by general practitioners as hopeless cases for treatment from the point of view of producing menstruation or pregnancy owing to the absence of the uterus.

The Goldberg-Maxwell syndrome comprises a very distinctive group of patients in whom the bodily habitus and sexual behaviour are essentially feminine. They are brought up as females, marry, and live as female partners. They consult the gynaecologist for primary amenorrhoea and sterility. The breasts are normal in size, but pubic and axillary hair is absent. The external genitalia—that is, the labia, urethra, clitoris, and vestibule—are normal in shape and situation. The vagina is of normal length and capacity; therefore there is no difficulty in coitus, and many of these patients are able to have orgasm. The vagina ends as a blind pouch, there being no cervix and uterus; although in some cases a fibro-fatty nodule or a vestigial uterus may be present.

The gonads are found in the abdomen, usually in the position of the ovaries, but may be situated elsewhere in the abdomen and attached to the posterior abdominal wall by a small mesentery. The broad and ovarian ligaments are absent or rudimentary. These gonads resemble an infantile type of ovary in appearance, being long, bulky, and lobulated. Cysts are sometimes present in their substance. On histological examination the gonads are found to be devoid of ovarian elements, but present the structure of immature, sterile, cryptorchid testes as typically found in the case reported in this article.

According to Goldberg and Maxwell, the urinary F.S.H. output is high (at least 96 M.U. in 24 hours), indicating primary gonadal deficiency; and 17-ketosteroid output is within normal range. Vaginal smears indicate a fair degree of oestrogenic stimulation of vaginal mucosa.

It has been said that the absence of pubic and axillary hair is a genetic abnormality comparable to the various congenital abnormalities found in ovarian agenesis or Turner's syndrome. Another feature of the Goldberg-Maxwell syndrome is the very strong family incidence, as will be obvious from the above case report of three sisters and from Schneider's cases, six of which occurred in one family and were spread over three generations.

Although some authors advocate the removal of gonads for fear of occurrence of neoplasm in cryptorchid testes, this point is highly debatable. Removal of these gonads may lead to unpleasant climacteric disturbances, as the gonads are responsible for the production of oestrogens, and not the adrenal cortex as thought by some. For this reason the syndrome has also been described under the heading of "oestrogen-producing testes." Adrenocortical function has been tested in various ways in these cases, but impairment of function of adrenal glands has not been found.

The nuclear sex of these cases is male. Jost and other workers have carried out certain experiments on animals by which they explain the occurrence of male nuclear patterns in these anatomically female cases. They postulate the

female form to be the basic or neuter, and the male differentiation to occur only in the presence of functioning testes during development of the embryo. Graham, in his experimental study in cats, has pointed out that sex chromatin can be recognized in the early embryo before the gonads have appeared, and therefore the sex is genetically determined and does not depend upon the hormonal status of the individual. Hoffenberg and Jackson have explained the varieties of gonadal dysgenesis and the various forms of human intersex by postulating three closely connected genes situated on the same chromosome. These authors have postulated one gene for infantilism or intrauterine hypogonadism—called "I"; one gene for shortness of stature, "S"; and one gene-complex for various anomalies of vegetative system called "A." According to them, the infantilism in gonadal dysgenesis results from very early failure of the developing gonad (their factor I), with consequent feminization of genital tract and body form. If gonadal dysgenesis occurs at a later stage of the male embryonic development, partial development along masculine lines will already have taken place. Further development of the genital tract will be of the female type, and thus "male pseudohermaphroditism" will result. This is equivalent to their "I" factor coming into operation at a slightly later stage. They conclude thus: "I" alone (slightly later in genetic male)—male pseudohermaphroditism; "I" (slightly later in genetic male) + S + A—male pseudohermaphroditism with short stature and anomalies.

The observations of Jost and Graham have led to the adoption of the term "gonadal dysgenesis" in preference to "ovarian agenesis." It also suggests that the Goldberg–Maxwell syndrome is, in fact, a variety of gonadal dysgenesis, where genetic development has failed in its attempt to produce a normally functioning testis and therefore the basic female pattern has continued. In this syndrome the failure to develop has probably occurred at a very early stage of development of the embryo, with the emergence of a complete feminine form and none of the male features. We can therefore say that the Goldberg–Maxwell syndrome is the earliest form of male pseudohermaphroditism.

Summary

The syndrome of Goldberg and Maxwell occurring in three sisters has been described.

The various features of the syndrome have been surveyed in detail.

The genetic aspects of the syndrome have been discussed in the light of modern work, and a hypothesis is produced to account for the syndrome.

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AN ERYTHROPOIETIC FACTOR PRODUCED IN THE KIDNEY

PRELIMINARY REPORT

BY

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A systematic study has been made of the response in mice to *x*-irradiation of the kidneys. The exteriorized kidneys were exposed to a single *x*-ray irradiation. The doses ranged between 100 and 18,000 r. By irradiation of the kidneys in mice a condition was produced resembling the essential features of glomerulonephritis in man with increasing nitrogen accumulation in the blood, anaemia, acidosis, oedema, hypertonia with hypertrophy of the heart, atrophy and granulation of the kidneys, albuminuria, haematuria, cast formation, decreased concentration of the urine to isosthenuria, and final collapse in a uraemic condition.

Experimental Findings

After 8,000 to 12,000 r increased blood pressure was observed in 10 days, whereas after 1,000 r about 8–12 months was necessary for this development. After unilateral nephrectomy and irradiation of the remaining kidney with 500 r the blood urea level increased in the course of five months. With the same procedure, and using 8,000 r, a rise in blood urea was observed after five days.

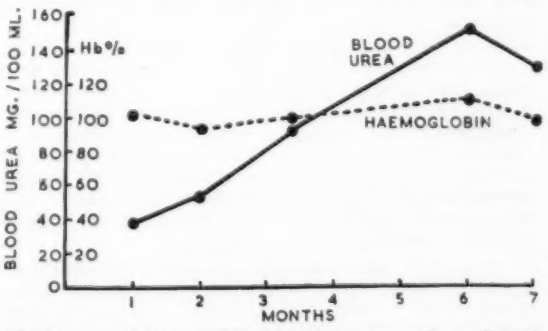
The anaemia caused by *x*-ray irradiation of the kidneys in mice was hypochromic to normochromic. The bone marrow showed a hypoplastic erythropoiesis.

In experiments with irradiation of the total amount of kidney tissue, the first changes observed were an increase of the blood urea level and a decrease in the haemoglobin values. Even at a time when the rise in blood urea was only from 20 to 23–24 mg. per 100 ml., a decrease in the haemoglobin value could be traced. It is therefore unlikely that the former caused the latter.

Through variation of the experimental procedure it has been possible to demonstrate the following.

1. In mice having a very small amount of kidney tissue shielded during the irradiation, the haemoglobin is maintained at a higher level than that usually found in connexion with the increased blood urea figures observed in these animals, and higher than in the animals with all the kidney tissue irradiated.

2. If one-quarter to one-third of one kidney is shielded during the irradiation the haemoglobin values may be maintained at the normal level, in spite of the development of



Blood urea and haemoglobin values in a mouse after unilateral nephrectomy and irradiation of approximately three-quarters of the remaining kidney with 8,000 r.

a considerable uraemia. The Chart shows the blood urea and the haemoglobin values in an animal which had been subjected to unilateral nephrectomy and irradiation of approximately three-quarters of the remaining kidney with 8,000 r. After six months the blood urea had reached 153 mg. per 100 ml., whereas the haemoglobin value was in the normal range, actually 111%.

3. Irradiation of one kidney and formation of an intraperitoneal outlet of the ureter from the other non-irradiated kidney is associated with normal haemoglobin values.

These experiments indicate that the failure of the kidney as an excretory organ and the development of the anaemia are parallel phenomena and independent of each other. These experiments also indicate that the kidney produces a principle of importance in erythropoiesis.

Table I gives the reticulocyte counts in (*a*) mice with both ureters ligated, (*b*) mice with total nephrectomy, (*c*) mice with partial nephrectomy, and (*d*) normal mice with intact kidneys. In all the groups acute anaemia was produced through bleeding. No reticulocyte reaction was found in the nephrectomized animals, whereas a reticulocytosis developed in the animals with ligated ureters. These observations correspond well with the findings of Jacobson *et al.*

TABLE I.—*Reticulocyte Count in Mice Bled ("Stimulus") in Connexion with Different Operations*

Operation	Stimulus	Reticulocytes %					Hb % 6 Days after Operation
		Before Operation	After Operation				
			12 Hours	24 Hours	2 Days	6 Days	
Ligation of ureters ..	Bleeding	2·7		4·7	Dead		
Total nephrectomy ..	,,	2·1	2·3	2·2	,,		
Partial nephrectomy (half a kidney left intact) ..	,,	2·0	4·2	5·9	7·0	21·3	48
Controls. No operation	,,	2·9	6·5	13·0	13·2	32·1	50

Each group comprises three mice.

TABLE II.—*Reticulocyte Count in Serum-injected Mice*

Condition of Experimental Animals	Stimulus	Reticulocytes %					
		Before Serum Inj.	After Serum Injection				
			1 Day	4 Days	6 Days	8 Days	10 Days
(A) Uraemic mice with anaemia (irradiated kidneys)	"Activated" serum	2·7	6·3	7·8	8·4	6·2	
(B) Normal mice	,,	2·4		4·0	4·7	3·4	1·6
(C) Nephrectomized mice	Bleeding "activated" serum	2·6	4·3	Dead			
(D) Uraemic mice with anaemia (irradiated kidneys)	Ultra filtrate of "activated" serum	2·4		7·5	9·3	12·7	9·7

Each group includes three to five mice.

(1957), who studied the erythropoietic titre in rats and rabbits, nephrectomized or with ligated ureters. The reticulocyte reaction seemed to be stronger in the animals with intact kidneys than in those with reduced kidney substance.

Serum from bled normal mice ("activated" serum) injected into mice with anaemia after irradiation of their total kidney mass produces reticulocytosis. As shown in Table II A, the reticulocyte response is considerable, in spite of a severe uraemia and acidosis, even after a single injection of "activated" serum (0.3 ml.). These experiments show that the bone marrow of uraemic mice responds to an erythropoietic principle present in the blood of bled animals. This erythropoietic principle is able to counteract the anaemia caused by irradiation damage in kidneys.

"Activated" serum will also produce a reticulocyte response in normal mice with normal haemoglobin values (Table II B). This observation may explain the polycythaemia sometimes seen in connexion with renal tumours, and it may indicate that the principle observed may be a factor of importance also for the normal erythropoiesis.

As mentioned above, after an acute haemorrhage no reticulocyte response is found in nephrectomized mice. If the nephrectomized animals are injected with "activated" serum a reticulocyte response develops (Table II C).

Table II D summarizes the results of experiments with injection of protein-free ultrafiltrate from "activated" serum into mice with anaemia after irradiation of the kidneys. Also this protein-free filtrate contains an active principle.

Conclusion

An attempt has been made to demonstrate morphological structures, which may be related to the functional findings recorded above. In normal mouse kidneys stained with crystal violet and light green (Wilson, 1952) the juxtaglomerular cells show definite granules. In mice with anaemia produced through daily bleeding there is in some instances a distinct reduction of the number of granules in the juxtaglomerular cells and diminution of the individual granules.

Some months after unilateral nephrectomy and *x*-ray irradiation of the greater part of the other kidney no granules are found in the juxtaglomerular cells in the non-irradiated part of the kidney, and none or very few and small granules in the irradiated part. In bilaterally irradiated kidneys the granules in the juxtaglomerular cells are well preserved and the cells may even appear to be increased in size, with enlargement of the individual granules.

Further studies of the possible relationship between the alteration of the granules in the juxtaglomerular cells and the erythropoiesis are in progress.

ADDENDUM.—Since erythropoietin is regarded as a protein or a protein-bound non-filterable principle, and since the ultrafiltrate of "activated" serum is effective in anaemic mice with irradiation-induced nephritis but gives no reticulocytosis in normal mice, the indication is that the substance active in nephritic mice is different from erythropoietin. It can also be demonstrated that the serum from nephritic mice with anaemia can induce reticulocytosis in normal mice (erythropoietin effect). Further investigations indicate that the erythropoietic principle which is active in nephritic mice is connected to the granules of the juxtaglomerular cells. Such a substance may be referred to by the name of "juxtaglomerulin." A detailed account will be published later.

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A proposal that W.H.O. should be asked to consider organizing an International Public Health and Medical Research Year was unanimously endorsed by the U.N. General Assembly's social, humanitarian, and cultural committee in New York on November 12. The committee adopted a resolution under which the Assembly would invite W.H.O., in accordance with its agreement with the United Nations, to consider a recommendation to organize the Year and to adopt ways of intensifying international co-operation in health matters. Under the finally adopted resolution, the Assembly would state its desire to combat widely prevalent diseases such as malaria, tuberculosis, smallpox, cholera, cancer, cardiovascular ailments, leprosy, and poliomyelitis, and to solve other serious health problems. The resolution, after noting other fields of effort such as the use of atomic energy in medicine and popular health education where international co-operation might be intensified, invites W.H.O. to inform the next General Assembly session (in 1959) of its reaction to these proposals.

HAEMOGLOBIN-H DISEASE

BY

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Haemoglobin-H was first described in 1955 by Rigas, Koler, and Osgood. It differs from the other abnormal haemoglobins so far described in that its inheritance cannot be followed by electrophoresis in its heterozygous and homozygous forms. Usually in the haemoglobinopathies, adult haemoglobin (HbA) and the abnormal haemoglobin are present in approximately equal quantities in the heterozygous state. In the homozygous state all or nearly all the haemoglobin present is of the abnormal type, the patient showing the features of the appropriate disease. In patients with haemoglobin-H disease the proportion of abnormal haemoglobin found varies from about 10 to 35%. It is irregularly found in relatives of these patients. In both these respects it resembles the appearance of haemoglobin-F in thalassaemia. Clinically, haemoglobin-H disease is very similar to thalassaemia minor. Two cases of this rare disease are reported in which red-cell survival and marrow iron turnover have been studied.

Methods

1. *Electrophoresis* of haemoglobins was carried out on Whatman No. 1 and No. 31 extra thick chromatography papers, using a horizontal technique in barbiturate buffer *p*H 8.6, M=0.05. By this technique HbA_2 can be separated from HbA.

2. *Red-cell survival time* was estimated using the patient's own cells labelled with radioactive chromium (^{51}Cr) as described by Joske, McAlister, and Prankerd (1956).

3. *The radioactive iron* (^{59}Fe) turnover was studied by the technique described by Harris, McAlister, Prankerd, and Singh (1957).

4. The foetal haemoglobin (HbF) percentage was estimated by the method of Singer, Chernoff, and Singer (1951).

Identification of Haemoglobin-H.—The abnormal haemoglobin found in the cases described was identified by comparison with a sample kindly supplied by Dr. J. C. White and by moving boundary electrophoresis carried out by Dr. E. M. Shooter and Mr. R. E. Skinner.

Case Reports

Case 1.—A Greek Cypriot, aged 23 years, living in London, attended hospital complaining of occasional nocturnal epileptic fits. He had always been pale and had had a few attacks of jaundice. When he was 7 years old he was treated in a sanatorium for tuberculosis. On examination the only abnormal physical signs were pallor, slightly icteric conjunctivae, and a just palpable spleen. When he was first seen his reticulocyte count was 7.5%. This gradually fell to normal at the time of the radioactive studies.

Case 2.—A Greek Cypriot woman, aged 22 years, living in London, attended hospital complaining of feeling unduly tired and weak during the past two years. On examination there were no abnormal physical signs apart from slight pallor. Her spleen was not palpable.

The investigations in both cases are set out in the table below.

Analysis of the Cases

	Case 1	Case 2
Haemoglobin	11 g./100 ml.	10 g./100 ml.
Red cell count	5·9 m./c.mm.	4·9 m./c.mm.
Packed cell volume	39%	37%
Mean cell diameter	7·7 μ	7·4 μ
,, haemoglobin concentration	28 g./100 ml.	25 g./100 ml.
Mean cell volume	66 cubic microns	75 cubic microns
,, average thickness	1·4 μ	1·7 μ
Reticulocytes	7·5%–2%	3·5%
Blood film	Marked variation in size and shape. No target cells.	Marked variation in size and shape. No target cells.
Red cell osmotic fragility. (Normal range, 0·48–0·30% saline)	0·42–0·21% saline	0·45–0·24% saline
Foetal haemoglobin	3·3%	3·2%
Schumm's test	Positive	Positive
Direct van den Bergh	Negative	Negative
Total plasma bilirubin	1·3 mg./100 ml.	0·5 mg./100 ml.
Urinary urobilinogen (Schlesinger's test)	Slight excess	No excess
Radiographs	Skull: normal Skeleton: normal	Skull: normal Humerus: normal

Results of Radioactive Iron and Chromium Studies

Figs. 1 and 2 show the results of these analyses. The uptake of ^{59}Fe was reduced over the marrow sites in the fourth and fifth lumbar vertebrae, but was increased in the shafts of the long bones. These results are interpreted as showing a reduction in marrow activity per unit volume of marrow, but an increase in total marrow volume due to peripheral spread in the skeleton. The reduction in marrow activity was more pronounced in Case 1. In both cases the ^{59}Fe uptake over the spleen and liver showed no evidence of extramedullary red cell production. The rate of ^{59}Fe appearance in the red cells was slightly increased—$T\frac{1}{2}$* Case 1=3.0 days, Case 2=2.7 days (normal=3.1 ±0.2 days)—indicating a slightly increased output of red cells.

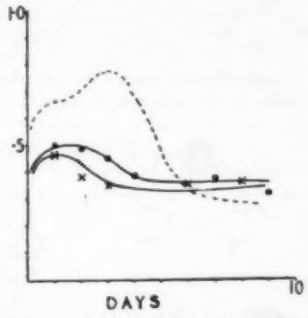

FIG. 1.—Uptake of ^{59}Fe measured as relative activity over L. 4 and 5. Vertical axis=Relative units of radioactivity. ×——×=Case 1. ●——●=Case 2. -----=Normal.

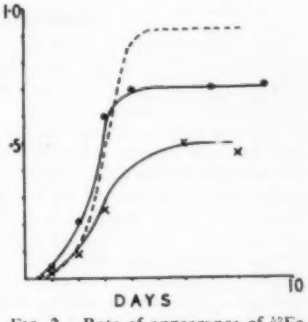

FIG. 2.—Rate of appearance of ^{59}Fe in red cells. Vertical axis=Fraction of injected ^{59}Fe in red cells. ×——×=Case 1. ●——●=Case 2. -----=Normal.

The ^{51}Cr survival time of red cells was slightly reduced in Case 2—$T\frac{1}{2}$†=13 days (normal 22–24 days)—and the mean cell life may be calculated to be about 70 days. There was no evidence of any excessive red cell destruction in the spleen. In Case 1 the ^{51}Cr survival time of the red cells was almost normal—$T\frac{1}{2}$†=20 days—but earlier there had been undoubted indirect evidence of haemolysis.

The Family of Case 1

1. Aged 68. Her blood contained about 10% of haemoglobin-H and she had the clinical and haematological picture of haemoglobin-H disease. Haemoglobin 9 g./100 ml.
2. Deceased.

*Half the time taken for the radioactive iron in the red cells to reach equilibrium.

†Half the time taken for the disappearance of radioactive chromium from the peripheral blood.

3. No abnormality found on clinical and haematological examination. Osmotic fragility of red cells within normal limits. Foetal haemoglobin 2% of total.

4. No abnormality on clinical and haematological examination. Osmotic fragility of red cells was within normal limits. Foetal haemoglobin less than 2% of total.

5. Case 1, described.

6 and 7. No haemoglobin-H found on paper electrophoresis. Foetal haemoglobin less than 2% of total.

Paper electrophoresis did not show any increase of HbA_2 in any of the relatives of Case 1.

The Family of Case 2

1. Paper electrophoresis showed no haemoglobin-H. Haemoglobin 8.9 g./100 ml. This anaemia responded to the administration of iron, her haemoglobin rising to 12 g./100 ml. Foetal haemoglobin 2% of total.

2. Not examined.

3. Electrophoresis showed haemoglobins A and H. She was suffering from a mild anaemia, similar to Case 2; haemoglobin 10.4 g./100 ml. Occasional target cells seen in blood film. Foetal haemoglobin less than 2% of total.

4. Case 2, described.

5. Not examined.

6. Paper electrophoresis showed no haemoglobin-H. Foetal haemoglobin less than 2% of total.

7. Paper electrophoresis showed no haemoglobin-H. Foetal haemoglobin 5% of total. (Child aged 1½ years; haemoglobin 13 g./100 ml.; normal red cell fragility.)

Paper electrophoresis did not show any increase of HbA_2 in any of the relatives of Case 2.

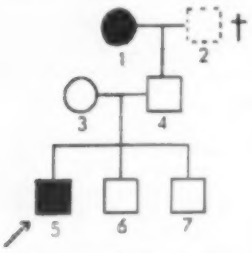

FIG. 3.—Family tree of Case 1.

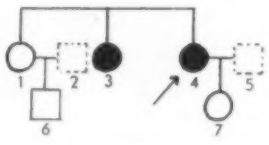

FIG. 4.—Family tree of Case 2.

Discussion

The results described show that haemoglobin-H disease is characterized by a slight reduction in the life span of red cells which is not associated with splenic destruction. There is a decrease in marrow activity, which is compensated for by marrow extension, and this results in a slight increase in total red cell output. Output, however, does not compensate completely for haemolysis. The life span of red cells appears to be variable, as a patient who at one time showed clear evidence of haemolysis later had an almost normal cell survival. These findings are similar to those in thalassaemia (Bailey and Prankerd, 1958), which the disease closely resembles in clinical features and haematological findings. However, it differs from thalassaemia minor in that HbA_2 is not increased in the patients or their relatives (Vella, Wells, Ager, and Lehmann, 1958). The cases so far reported have been from races in which thalassaemia occurs (Vella *et al.*, 1958); and Motulsky (1956) states that haemoglobin-H disease is the result of the interaction of the thalassaemia and "H" genes. Our two families show no evidence to support this theory, as none of the relatives have thalassaemia.

Summary

Four cases of haemoglobin-H disease are reported from two Greek Cypriot families living in London. One case from each family has been studied in detail, and results of red cell survival time and marrow iron turnover are presented. The familial nature of the disease is demonstrated.

We are grateful to Dr. E. A. Blake Pritchard for permission to study and publish Case 1.

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TOXIC PSYCHOSIS FOLLOWING ATROPINE EYE-DROPS

BY

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It is well known that atropine may produce a delirium in addition to its more characteristic autonomic effects, and that in certain sensitive subjects these effects will arise with normal pharmacological doses. It is less well known that atropine can produce delirious states with minor or absent peripheral signs of intoxication and that severe mental reactions can follow routine instillation of atropine eye-drops.

The case described is one of acute toxic psychosis caused by routine atropinization of the right eye over a period of three and a half weeks in the course of treatment of retinal detachment.

The condition is rare in adults and few cases have been reported in the literature (Hopkins and Robyns-Jones, 1937; Listwan and Whealy, 1953; Schinko, 1954), but it is suggested that milder degrees of mental disturbance often seen after eye surgery and attributed to emotional stress of the post-operative regime may be due in part to atropine intoxication.

Case Report

The patient was a married woman of 33, without children, intelligent, and described by her family as somewhat highly strung, emotional, and imaginative. After the death of her father two years ago she had spent three days in a neurosis unit, the diagnosis being reactive depression with hysterical features. There was a similar episode 11 years ago after the death of her first husband, but without admission to hospital.

The medical history included rheumatic fever at the age of 12, followed by a slight persistent tachycardia, and myopia requiring 10 dioptres correction. She had recently worn contact lenses. There was no significant family history.

On June 29, 1957, she was admitted to Moorfields Annexe, Highgate, with a right temporal retinal detachment. Treatment with bed rest, double eye pads, and daily instillations of 1% atropine sulphate drops was instituted. On July 4 she was transferred to Moorfields Hospital, where the atropine drops were instilled twice daily. At this time she was judged to be "unstable in temperament," and phenobarbitone, ¼ gr. (32 mg.) t.d.s., was added to her treatment.

Diathermy and subretinal aspiration was performed on July 8 under thiopentone, gallamine triethiodide, gas and oxygen, with premedication by "omnopon" and scopolamine. There were no complications. Atropine drops twice daily, eye pads, and strict bed rest were continued until July 19, when masked glasses were substituted for the pads.

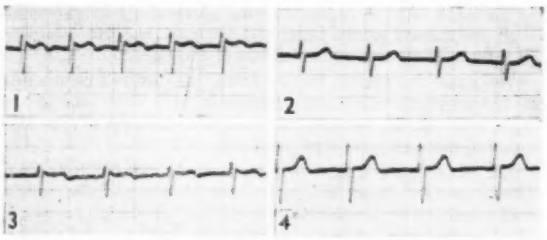
more liberty of movement was allowed in bed, and the phenobarbitone was replaced by chlorpromazine, 25 mg. t.d.s.

Over the next four days she became increasingly noisy, disorientated, and irrational, and required oral and intramuscular barbiturates. By July 23 she was quite unmanageable and was transferred to Three Counties Hospital on an Urgency Order.

On admission she was disorientated in time and place, was amnesic for recent events, mistook identities, and asked if she was to have an operation. She was restless and garrulous, refused to stay in bed, called out in terror, and at times wept uncontrollably. She stated that she had seen the Cross and "boats to sail away in," and had heard the voices of near relatives. She believed people to be talking about her and plotting against her. At times she showed partial insight.

On examination she was of average physique; the right pupil was fully dilated and the left less so and reacting to light; the gait was slightly ataxic; there was a tachycardia of 150 a minute, and the blood pressure was 170/90. There were no other abnormal physical findings.

Next day her mental state had deteriorated. She was resistive and hostile, offered violence, was incontinent, and refused food. This state was not continuous, but was broken by more lucid intervals, during one of which she was sufficiently quiet for an E.C.G. tracing to be taken. This showed (first tracing in Figure) a regular sinus tachycardia,



E.C.G. Lead V_5. (1) On admission (July 24). (2) At 11 a.m. on August 13. (3) At 3.45 p.m. on August 13—atropine sulphate, 1/66 gr. (1 mg.), given at 11.10 a.m. (4) At 6.45 p.m. on August 13—neostigmine, 1 mg., given at 4 p.m.

rate 130, with diphasic T wave throughout the chest leads and some elevation of the ST segment. The white-cell count was 15,000, with a polymorphonuclear leucocytosis; Hb, 102%; W.R. negative; E.S.R. 7 mm./hr.; urine, N.A.D.; chest *x*-ray examination N.A.D.

At this stage the diagnosis lay between an acute schizophrenic reaction and a toxic delirium, the latter being more probable because of the lucid intervals, visual hallucinations, and disorientation, together with the myocardial findings. It was tentatively suggested that the condition might be due to atropine poisoning, but this was discounted by outside medical opinion; for fear of neglecting the post-operative care of the eye the drops were continued.

By July 25, despite sedation, her mental condition had deteriorated further and tube feeding had to be instituted. Electroplexy was considered, but thought to be too dangerous in view of the toxic state of the myocardium. The pulse rate remained at approximately 150. It was decided to discontinue atropine, and within 24 hours there was some improvement in her mental state.

After 48 hours the pulse rate had fallen to 96, but mentally she was relapsing again and refusing nourishment. It was now thought that her myocardial condition had improved enough to allow electroplexy, which was indicated by her continued overactivity, resistiveness, and refusal to take nourishment. Daily E.C.T. was given until July 30, by which time she had greatly improved, was normal in behaviour and mood, and had no disturbance of cognitive function. Over the next few days, however, she again became more labile emotionally, rather demanding and querulous, and was expressing paranoid ideas.

By August 6 she had gained in insight and was more settled, but still emotionally unstable and liable to tears. On the 8th a suture was removed from the eye by our visiting ophthalmic surgeon and a satisfactory report given on the state of the retina. An E.C.G. tracing taken on August 9 was within normal limits, rate 96.

In view of the possibility that this patient might need further treatment to her eyes in the future, it was considered important to assess the part played by atropine in the aetiology of her psychosis, so on August 9 an injection of atropine sulphate, 1/100 gr. (0.65 mg.) was given subcutaneously, with the suggestion that it was a sedative. Six hours later she developed a garrulous, emotional, paranoid, hallucinated state resembling in lesser degree her condition of the previous week. Systemic effects were negligible. Unfortunately she was too uncooperative to permit a further E.C.G. being taken. Next morning she was more settled, but still showed some pressure of ideas and a tendency to form illusions.

In order to eliminate the possibility that this was a chance relapse, and if possible to have electrocardiographic confirmation of the effects of atropine, a further trial dose of the drug, this time 1/66 gr. (1 mg.), was given subcutaneously at 11.10 a.m. on August 13, again with the suggestion that it was a sedative. An E.C.G. was taken (second tracing in Figure) 10 minutes before the injection and was normal, rate 96. By midday she showed pressure of ideas and increased lability of affect, but no significant systemic effects or alteration of the pulse rate. By 2 p.m. she complained of a burning sensation in the palms of her hands and in her brain, and said she felt she could no longer contain herself or suppress her feelings. She began to make absurd accusations against the hospital and demanded her immediate discharge on the grounds that her room was a locked cell (untrue) and that the tea was not strong enough. She asserted that patients were being given nicotine injections to make them cough, and that others were being gassed. She could smell the gas (not true) and insisted that she could hear men laughing, her sister's voice, and the click of billiard balls. Visual hallucinations were also suspected.

An E.C.G. taken at 3.45 p.m. (third tracing in Figure) showed the same slight elevation of the ST segment and diphasic T wave as in the tracing taken on admission (first tracing in Figure). There was no increase in sinus rate.

At 4 p.m. 1 mg. of neostigmine was given, and a further E.C.G. taken at 6.45 p.m. (tracing 4 in Figure) showed that the myocardial changes produced by the atropine had resolved. Her mental condition, however, did not settle markedly until next morning, and not completely until three days later.

She was discharged on August 16, and has since remained well and has returned to work.

Discussion

Listwan and Whealy (1953) described the characteristic mental symptoms of atropine intoxication as a confusional state with vivid visual hallucinations, restlessness, muscular incoordination, and later increased emotionalism with a short period of retrograde amnesia. In our case all these features were present together with aural and olfactory hallucinations. Peripheral post-ganglionic cholinergic effects were minimal apart from the tachycardia on admission. It is thought that the E.C.G. changes were due to direct action on the myocardium, as in the model psychosis there was no increase in sinus rate.

Fleury and Marx (1949) pointed out that intoxication is not due to transconjunctival absorption but to the swallowing of atropine-laden tears. In 1% atropine sulphate, each drop contains 1/110 gr. (0.6 mg.). Assuming complete absorption, three drops in the normal subject will produce parasympathetic paralysis, six drops restlessness, and 15 drops mental symptoms and ataxia. In sensitive subjects

mental or peripheral symptoms will follow much smaller doses. Children (Tyson, 1889; Kelynack, 1890; Scally, 1936; Duggan, 1937; Belz, 1949; Fleury and Marx, 1949) and the elderly (Métivier, 1935) are particularly affected.

Recommendations to reduce the risk of side-effects from atropinization of the eye have included the use of a 0.5% solution, precautions to avoid concentration of the solution by evaporation, and compression of the internal angle of the eye to obstruct the lacrimal duct during instillation (Belz, 1949; Fleury and Marx, 1949).

It would be interesting to know if any positive correlation could be found between the more minor emotional disturbances and restlessness which often accompany eye surgery, and any particular dosage or method of atropine administration.

Summary

A case is described in which an acute confusional psychosis resulted from the routine administration of 1% atropine sulphate drops in the treatment of retinal detachment. The psychosis was accompanied by myocardial changes giving rise to considerable concern. Other peripheral signs of atropine intoxication were absent. A remission of the confusional state followed discontinuation of the eye-drops and a short course of electroplexy; paranoid trends and emotional lability persisted for a further few days.

At a later date, in order to establish a diagnosis, small test doses of atropine were given by injection. Both the psychotic symptoms and the myocardial change seen when the patient was having atropine eye-drops were reproduced.

The literature concerning mental symptoms following the use of atropine eye-drops is reviewed and possible preventive measures against intoxication are described.

It is suggested that closer investigation might be made into the origin of states of minor emotional disturbance, usually attributed to psychological stress, in patients undergoing eye surgery with prolonged routine atropinization. E.C.G. changes appear to be useful in establishing a diagnosis of atropine sensitivity where other peripheral signs of intoxication are lacking.

Our thanks are due to Dr. Leslie Ford, medical superintendent of Three Counties Hospital, for permission to publish this case, to Dr. L. G. M. Page, deputy medical superintendent, for his help and advice, and to Dr. D. W. Hill for details of treatment at Moorfields Eye Hospital.

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Opening a conference on cerebral palsy, held in London on November 21 by the British Council for the Welfare of Spastics, Mr. R. H. M. THOMPSON, Parliamentary Secretary to the Ministry of Health, said that the overall needs of children and young people suffering from cerebral palsy were early ascertainment, full assessment, expert treatment, education, training for future employment, and continuing aftercare in the community. At the same time the parents needed guidance in the child's home management, and help in coping with their own numerous practical and personal problems. The need was to build up a system of comprehensive care available to sufferers throughout their lives. Mr. Thompson thought the greatest need was for further understanding of the causation of the disease, for it was only in this way that we could prevent it. Research into its causation and treatment would ultimately be of benefit to children suffering from other handicaps also.

RENAL COLIC AND ANURIA FROM ACETAZOLAMIDE

BY

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Acetazolamide, "diamox," is a sulphonamide derivative and inactivates carbonic anhydrase. By oral administration it is rapidly absorbed, and is excreted largely unchanged by the kidney within 6–12 hours. The inhibition of carbonic anhydrase leads to increase of sodium bicarbonate in the urine and increased potassium output.

Acetazolamide is widely used for glaucoma and as a diuretic in cardiac disease, and is reputedly very free from serious complications; only three papers have appeared in America reporting complications and none at all in Great Britain, which is the reason for the publication of this case.

Case Report

The patient, a man aged 54, was quite well until 5.30 p.m. on May 1, 1958, when he passed urine normally. Shortly afterwards urgency developed and a quantity of "very thick urine" was passed with pain. Pain then developed in the right loin; it radiated to the groin and was associated with frequency, penile pain, and haematuria. He was seen by Dr. J. Williams, who diagnosed renal colic.

Next day the patient voided 15 oz. (425 ml.) of clear urine in the morning and complained only of a dull ache in the right loin. Later, severe low back pain developed with left-sided abdominal pain and vomiting.

On May 3 the severe low back pain and vomiting continued and no urine was passed for 24 hours. The patient was admitted to Leatherhead Hospital; temperature 99° F. (37.2° C.). No stones were seen by straight radiograph. Cystoscopy (lignocaine gel analgesia) showed the bladder to be empty but otherwise normal. The right ureter was inactive and a catheter could not be passed beyond 1 cm. The left ureter was obstructed at 5 cm., but a catheter with stylet was successfully forced through and bloody urine poured down the ureteric catheter under considerable pressure.

The ureteric catheter was tied in and 38 oz. (1,077 ml.) drained through it during the night. Distaquaine penicillin, 300,000 units, was given daily for six days from May 3. Sulphonamide crystalluria was diagnosed, and sodium bicarbonate, 60 gr. (4 g.) 4-hourly, was given orally and intravenous saline discontinued early, as the patient took well by mouth.

On May 4 the blood urea was 95 mg. per 100 ml.; plasma CO_2, 16.1 mEq/l.; serum chlorides, 106 mEq/l.; sodium, 139 mEq/l.; potassium, 4.6 mEq/l. Urine: bladder and left ureter, sterile; red cells ++; no crystals.

Progress was satisfactory; urine drained well from the ureteric catheter and the left renal pain was relieved at once. After about 12 hours the patient voided a few ounces of urine around the catheter; this was thought to be from the right kidney, as relief of right renal pain then occurred. The blood pressure was 150/85. The ureteric catheter was removed on May 6 after retrograde pyelography had shown a curious beaded appearance at the lower end of the ureter which might have been due to oedema or collections of crystals. The blood urea had fallen to 72 mg./100 ml.

The following day the patient was passing clear urine, but a peak of temperature followed, due to pyocyaneus infection of the urine, which responded well to a five-day course of chloramphenicol.

On May 18 the patient was discharged well with a blood urea of 29 mg./100 ml.

Discussion

The diagnosis of this case lay between bilateral non-opaque ureteric calculi and crystalluria. The obstruction to the ureteric catheter very closely resembled the blockage experienced in sulphonamide crystalluria.

It was known that the patient had attended elsewhere for blurred vision (? glaucoma) in the left eye; he had improved somewhat on 2% pilocarpine, and was then given acetazolamide as follows: Two tablets on April 25, 26, 27, and 28, none on the 29th, two on the 30th, and one on May 1. The thick urine appeared during the evening of May 1 and was rapidly followed by bilateral renal colic and anuria; it seemed reasonable, therefore, to blame the tablets. Advice was sought from various medical colleagues, and it was concluded that the patient might have been taking sulphonamide tablets instead of the "harmless diuretic" acetazolamide.

Mr. C. R. Davenport, senior pharmacist at King's College Hospital, pointed out the sulphonamide nature of acetazolamide, of which I and most of my colleagues appeared to be ignorant. This seemed to clinch the diagnosis, and Messrs. Lederle, the manufacturers, were contacted, and provided helpful information.

Dr. L. H. Worth reported the following case at the Royal Society of Medicine on February 28, 1956, but the account was not published.

A man, aged 47, was given acetazolamide, 1 tablet twice daily, for two weeks from January 13, 1956, and the dose was increased to 1 tablet thrice daily on January 27. From the evening of January 31 until his death on February 5 he had complete anuria. The bladder was empty and no urine was obtained by ureteric catheterization. No crystals were found to be obstructing the moderately distended and oedematous ureters.

The story in Dr. Worth's case closely resembles the story in the present case.

Persky, Chambers, and Potts (1956) report three cases of ureteric colic following acetazolamide administration. Stones were removed by cystoscopy from the ureter in two patients, and it was suspected that some had been voided naturally in the third. The stones were not analysed. All three patients voided an acid urine, which is against phosphaturia, and it is suggested that the suppression of citrate production was the cause.

Glushien and Fisher (1956) reported post-mortem findings on a man of 55 who had had 250 mg. of acetazolamide thrice daily for four days. The kidneys closely resembled those of patients "succumbing to sulphonamide intoxication," but there was no clinical evidence of renal failure or sulphonamide intoxication during life.

Summary

A case of renal colic and anuria due to acetazolamide is reported.

The condition resembles sulphonamide crystalluria and responds to treatment for that condition.

In no case have sulphonamide crystals been detected, nor has an expected phosphaturia been confirmed.

Further investigation on the urine of patients taking acetazolamide are being carried out and will be necessary to explain the mechanism of this rare but serious complication.

I wish to thank Dr. N. E. G. Richardson for her help in the pathological investigation and Mr. C. R. Davenport and Mr. J. R. Wilson for their help.

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Medical Memoranda

Value of Penthienate Methobromide in Lienteric Diarrhoea and Encopresis in Childhood

Penthienate methobromide ("monodral"), like other anticholinergic drugs, depresses the motility and secretion of the stomach and reduces the motor activity of the intestine. Its therapeutic value in the treatment of peptic ulcer and dyspepsia is accepted, but its value in the treatment of disorders of the small intestine and colon remains unproved. Nevertheless, Ingegno (1954) considers that penthienate can control diarrhoea in patients with an "irritable" or "spastic" colon. I have, however, been unable to find any reference to its use in cases of lienteric diarrhoea and faecal incontinence in childhood. For this reason I record the effect of the drug upon 28 children between 4 and 12 years of age who were suffering from one or both of these complaints.

MATERIAL AND METHOD

Of the 28 patients selected, 12 suffered from lienteric diarrhoea and 16 from faecal incontinence. The patients were seen in a hospital out-patient department, so that the diagnosis of the conditions was largely dependent upon the history and physical examination of each child. Urinalysis, radiological examination, E.S.R., and Mantoux tests were performed where they were considered necessary. Cases of incontinence due to indigestion or chronic constipation were excluded from the series. Twelve of the cases with encopresis probably also suffered from lienteric diarrhoea. To subdivide the group accurately would not be easy, nor would it serve any useful purpose.

Histories obtained from the 12 patients with lienteric diarrhoea showed that the condition had been present for periods varying from two months to three and a half years, and that nine of them had some degree of abdominal pain or discomfort from time to time. In the 16 cases of bowel incontinence the duration of symptoms varied from two months to five years, and 12 of them had diarrhoea and six had attacks of abdominal pain. Ten patients had urinary incontinence as well as faecal incontinence. In four of the 28 children, food, such as soup and fruit, could aggravate their condition. Five other patients were similarly affected by mental strain. In two cases the symptoms may have been partially due to difficulties in training, because one child was mentally retarded and the other was deaf. These factors, however, did not prevent penthienate from having some beneficial effect.

All the patients were treated in the hospital out-patient department. They were advised to take their usual diet, but the fluid intake of the 10 patients with both urinary and faecal incontinence was restricted. In each case penthienate was prescribed, a 5-mg. capsule to be taken two or three times a day after food. Treatment was continued for at least two months.

RESULTS

Of the 12 children with lienteric diarrhoea, 11 became asymptomatic. The patient who failed to respond to the specific treatment was admitted to hospital, where he immediately recovered with no medicine, presumably because of the change in his environment and mode of living. Of the 16 patients who were treated for encopresis, eight obtained relief, and eight partial relief of their complaint. Twelve of these patients also had diarrhoea, and this subsided completely in seven cases and diminished in severity in the remaining five. It is apparent that penthienate therapy benefited almost all of the 28 patients, the results being exceptionally good in those suffering from lienteric diarrhoea only and in half of those patients suffering from faecal incontinence. All but one case obtained some relief of their diarrhoea, and in some cases it was complete.

The influence of penthienate on abdominal pain, which was present in 15 out of the 28 patients, varied: in 10 out of the 15 the pain either disappeared or diminished, and in 5 the frequency and severity of the pain either continued

unaltered or became worse. The aggravation of the pain may have been due to the treatment, for two patients who had no abdominal pain or discomfort prior to penthienate therapy developed it while taking the drug.

Enuresis was noted in nine children. The response of this condition to penthienate was recorded: only one gained normal bladder control, in seven control of the bladder improved, and in one it remained unchanged. It would therefore seem that both abdominal pain and enuresis, when associated with either lienteric diarrhoea or encopresis, are likely to be alleviated by this treatment.

COMMENT

This paper does not describe a scientifically controlled investigation. Neither the methods of diagnosis of the conditions nor those of assessing the results of treatment fulfil the necessary conditions. Nevertheless, from a clinical point of view it is apparent that treatment of lienteric diarrhoea and faecal incontinence with penthienate leads to a marked improvement in most cases. The drug appears to be more effective than older methods of treatment, and when used alone or in conjunction with other remedies constitutes a definite advance in the treatment of these conditions.

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ADDENDUM.—Since this memorandum was submitted for publication three further cases of encopresis and diarrhoea have been treated with penthienate methobromide. In one the encopresis was abolished and in the other two it was greatly improved. The diarrhoea subsided in each case.

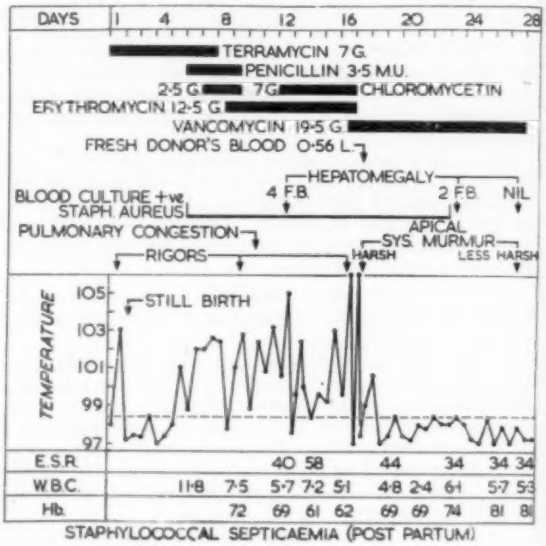
Resistant Staphylococcal Puerperal Septicaemia Susceptible to Vancomycin

The resistant staphylococcus has for some time been a commonplace in the hospital nursery, and has lately invaded the general surgical wards, causing severe, sometimes fatal, damage. Its spread to the parturient mother, though not yet generally publicized, is obviously only a matter of time, and with this in mind we have thought it might be useful to record our recent experience with such a case.

CASE REPORT

The patient, a 10-para aged 40, was admitted to hospital with ruptured membranes on February 3, 1958, 11 weeks before the expected date of delivery. She continued to drain clear liquor, but as labour did not begin spontaneously antibiotic therapy was instituted after two days with "crystamycin," 1 g. twice daily. There was no change until nine days later, when the patient suddenly complained of severe malaise, and had a rigor with a temperature of 104° F. (40° C.). As the symptoms pointed to an infection of the urinary tract treatment was changed to "sulphatriad" and potassium citrate in high dosage, but, despite the persistence of pyrexia, this was discontinued when the result of urine examination proved negative. Labour began the same evening. The foetal heart sounds had disappeared four hours previously. She was delivered five hours later of a stillborn foetus of 4 lb. 15 oz. (2,210 g.) showing early maceration. The delivery was spontaneous, with a normal and complete third stage. Oxytetracycline ("terramycin"), 250 mg., was given six-hourly, together with vitamin-B complex in high dosage, and the temperature remained normal over the next two days. It then suddenly shot up again, rapidly becoming established as a high fever ranging between 103 and 106° F. (38.9 and 41.1° C.) with subnormal intermissions. The clinical picture was that of a typical septicaemia with recurrent rigors, physical deterioration, liver enlargement, and anaemia. A vaginal swab and repeated blood cultures yielded a profuse growth of *Staphylococcus aureus* resistant to penicillin but sensitive to chloramphenicol and erythromycin. Appropriate combined chemotherapy, details of which are shown in the accompanying Chart, failed to produce any improvement; the septicaemic condition continued unchecked and there was clinical evidence of localization in the liver and on the heart valves as shown by hepatomegaly, and a harsh apical systolic murmur conducted into the axilla. The general condition of the patient rapidly deteriorated, with increasing hepatomegaly and incipient endocarditis, the E.S.R. remained high between 35 and 40 mm. (Westergren), the Hb percentage diminished from 84 to 57, and the cells showed marked toxic granulation.

At this stage it was decided to try the effect of the new antibiotic vancomycin, and, though not yet commercially available, a supply was obtained from the makers. The



STAPHYLOCOCCAL SEPTICAEMIA (POST PARTUM)

result was immediate and dramatic. After the second eight-hourly intravenous injection of 500 mg., the temperature fell to normal, and, except for a small peak the following day, remained permanently subnormal. Blood cultures became sterile after three days, and the blood picture returned to normal. All the clinical signs and symptoms regressed rapidly and completely, and there was no remission when the drug was discontinued after 10 days, the patient leaving hospital very fit and well after a further 10 days.

COMMENT

Vancomycin is a new antibiotic produced from *Streptomyces orientalis*, an organism found in some Indonesian soils. Fairbrother and Williams (1956) have shown that it is lethal *in vitro* to most strains of *Staph. aureus* resistant to other antibiotics. More important, bacterial resistance to it is apparently unknown (Garrod and Waterworth, 1956). Only a small number of clinical cases have so far been treated (Kirby and Divelbiss, 1957; Griffith and Peck, 1956), but its value, though still largely undocumented, appears to be established, and it would seem the ideal counter to the increasing bugbear of the resistant staphylococcus. It unfortunately has one grave disadvantage—that it can be administered only by the intravenous route.

Vancomycin is manufactured under the trade name of "vancocin" by Eli Lilly and Co. Ltd., and we are much indebted to Mr. Cooke, of this firm, for a generous supply of the drug. We also thank Mr. A. Dickson Wright and Dr. Geoffrey Konstam for clinical advice and help.

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Reviews

HARVEY TERCENTENARY CONGRESS

Circulation. Proceedings of the Harvey Tercentenary Congress. Edited by John McMichael, M.D., F.R.C.P., F.R.S. (Pp. 503+xxiii; illustrated. 50s.) Oxford: Blackwell Scientific Publications. 1958.

This book contains a summary of contributions made at the Harvey Tercentenary Congress last year. The standard of the contributions can be judged from the high international renown of all the contributors. The first part consists of eight short articles centred around Harvey himself, all of them very welcome to the medical historian. The main body of the book presents a most interesting cross-section of modern research on the circulation. It is only on seeing all the contributions to this congress collected together that one fully appreciates how successfully the celebrations were designed to bring out the protean forms of present-day research on the cardiovascular system. What is so striking is that all the contributions except three deal with the problems of blood flow, pressure, or resistance in the various circulations of the body. Harvey concerned himself directly with the question of cardiac output, and Stephen Hales, of Teddington, carried the matter further to quantitative estimation of systemic blood pressure. The largest part of the present work is devoted to the developments of just those problems of circulation which these two investigators originated. It is surprising to realize that these aspects of the circulation, which are indeed the next logical step from Harvey's own work, have had to wait for some 300 years for their further successful development.

It is a sign of our rapidly changing times that in such a book, summarizing present-day work on the heart and circulation, there is only one electrocardiogram and about a dozen radiographs. The large majority of the many illustrations concern haemodynamics and results of the application of the Fick principle. Thus, for those who wish to see where Harvey's original work leads, this book is of inestimable value. Incidentally, the quality of its production matches that of the contributions. Our gratitude to the Harveian Society, and in particular to Mr. Dickson Wright and Dr. Geraint James, for their inspired organization of these timely proceedings must be great indeed. Professor John McMichael has constructed an attractive book out of the varied historical and scientific contributions which constitutes at once a worthy and logical acknowledgment of Harvey's greatness.

K. D. KEELE.

ATOMIC ENERGY AND MENTAL HEALTH

Mental Health Aspects of the Peaceful Uses of Atomic Energy. Report of a Study Group. (Pp. 53. 3s. 6d.) Geneva: World Health Organization. 1958.

"This report contains the collective views of an international group of experts" that met in Geneva under the auspices of W.H.O. for nearly a week in October, 1957. Tribute is paid to the stimulus provided by the World Federation for Mental Health, whose executive board had approved a statement and adopted a resolution dealing with the same subject at a meeting held in London earlier in the year. (These are reprinted in two annexes.) Some—but by no means all—of the topics considered in the report proper may be indicated by the main sectional headings. These are: (1) the personal challenge of atomic energy; (2) the question of brain damage from radiation; (3) the socio-economic impact of atomic energy on mental health; (4) unhealthy emotional responses immediately provoked by the advent of atomic energy; (5) mental health tasks. The third annexe is entitled "The Press and Atomic Energy."

It will be seen that the study group did not feel narrowly confined as to what could profitably be discussed and promulgated. It is conceded that no one can predict with confidence what atomic developments may take place, nor what their effect might be upon both individuals and groups. But it is argued that, whilst the material world may change with dramatic rapidity, human nature—so long as humanity survives—is likely to remain much the same. A liability to irrational fears and irresponsible actions will continue, and may be further intensified by new and startling developments. The basic principles of mental hygiene will maintain their validity. For example, children should "have an upbringing free from anxiety and hate—producing in individuals self-reliance and a sense of responsibility towards others." Again, "the creation of good human relations in the family, the place of work and the community" is of fundamental importance, as is the "education in mental health requirements" amongst "those in responsible positions in public life."

Amongst the "specific suggestions" under the section "Mental Health Tasks" it is proposed "that in local areas small but highly qualified interdisciplinary teams should be formed consisting of, perhaps, a psychiatrist, a psychologist, a sociologist, and a journalist. The plan could be carried out in the central governmental organization as well as in the local district or community." The duties of such teams would include the study of local conditions and local mental health problems; advice—"having regard to modern techniques of vocational selection"—in the selection of the more highly responsible personnel of atomic installations; the instruction of such personnel and of atomic scientists in the "basic psychological principles of human relations"; and in general the education of the public with the assistance of "specialized journalists in human relations."

The report concludes with an oracular peroration: "But in the long run the greatest hope of mental health in the future of the peaceful uses of atomic energy is the raising of a new generation which has learnt to live on terms with ignorance and uncertainty and which, in the words of Joseph Addison, the eighteenth-century English poet, 'rides in the Whirl-wind, and directs the Storm.'"

DESMOND CURRAN.

ENDOCRINE PATHOLOGY OF OVARY

Endocrine Pathology of the Ovary. By John McLean Morris, M.D., and Robert E. Scully, M.D. (Pp. 151; illustrated. 63s.) London: Henry Kimpton. 1958.

Although it is common knowledge that granulosa-cell tumours of the ovary may produce oestrogens and arrhenoblastomas cause virilization, pathological secretion of hormones by the ovary in other circumstances, and the consequences that may ensue from this, are much less widely appreciated. The admirable monograph by Morris and Scully, two acknowledged experts in this field, should therefore fill an important gap in medical literature. Its purpose, as set out in the preface, is "to correlate the pathological changes occurring in the ovary with the accompanying clinical endocrine findings and to evaluate both in the light of the material available for study." In this it succeeds admirably. The book is beautifully produced, well documented, and illustrated with superb photomicrographs. It begins with a very clear account of the cells of the gonads, which is followed by a summary of their embryology and the part played by hormones in sexual differentiation. The remainder of the introduction is concerned with the currently available hormone assays and with a classification of endocrine effects. There follow sections on non-neoplastic abnormalities of the ovary producing endocrine effects; granulosa-theca-cell tumours; Sertoli–Leydig cell tumours; sex-chord mesenchyme and mixed-cell tumours; lipoid-cell tumours; germinomas, teratomas, and related tumours; and, finally, tumours with "functioning stroma." Everyone with an interest in ovarian pathology or in the endocrinology of the gonads can expect to read this book with enjoyment and profit.

G. I. M. SWYER.

LIPIDS AND ATHEROSCLEROSIS

Chemistry of Lipides as Related to Atherosclerosis. A Symposium. Edited by Irvine H. Page, M.D. (Pp. 342+xii; illustrated. 63s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1958.

This book is a manifestation of the great increase of interest in atherosclerosis. Various aetiological theories have been proposed, and one of the factors which has been incriminated is dietary fat. The possible aetiological importance of dietary fat and the experimental and clinical evidence for an association of hypercholesterolaemia with atherosclerosis have focused attention on lipid metabolism. The lipids are of major significance in the problems of atherosclerotic heart disease whether they are of primary or secondary aetiological importance. The time is ripe, therefore, for a concise but detailed account of the chemistry of the lipids in relation to atherosclerosis. This book fills the purpose admirably. It contains the proceedings of an international symposium held last year in the United States. The contents include chapters concerning the chemistry or metabolism of cholesterol, fatty acids, triglycerides, phospholipids, and sphingolipids. Perhaps chapters of greater medical interest are those concerning dietary fats and human lipid levels, unsaturated fatty acids in coronary disease, lipoprotein lipase and the nature of the lipaemia clearing reaction, lipoproteins, and the non-esterified fatty acids in plasma.

For those not specifically interested in the problems of atherosclerosis this monograph will, as the title implies, hold limited attraction; for them it is sufficient to quote a statement of practical policy from I. H. Page's well-balanced introduction: "The evidence at present does not convey any implications for drastic dietary change, specifically in the quantity or type of fat in the diet of the general population on the premise that such changes will definitely lessen the incidence of coronary artery disease." For those actively studying atherosclerosis this book should prove most rewarding, and reference will often be made to it.

M. F. OLIVER.

HYPNOTHERAPY

Hypnosis in Health and Sickness. By Gordon Ambrose, L.M.S.S.A., and George Newbold, M.B., B.Sc., M.R.C.S., M.M.S.A., D.R.C.O.G., D.C.H. (Pp. 196. 15s.) London: Staples Press Ltd. 1957.

When the great Liston saw the inhalation of ether producing surgical anaesthesia for the first time at University College Hospital in 1841 he is said to have remarked, "This beats mesmerism hollow." And it has been one of the tragedies of mesmerism and of hypnosis since then that, although sometimes very useful treatments, they have so often turned out to be only temporary palliatives for a wide range of ailments, for some of which better and more specific treatments are always in the process of being discovered. But exponents of hypnotism have never been backward in pressing its therapeutic virtues, and this has resulted in wave after wave of enthusiasm for mesmerism or hypnosis, always followed by profound disillusionment when it has become practised on too wide and indiscriminate a scale.

This particular book seems to be written more for the lay reader than the general practitioner and medical specialist. Note its style: "The cerebellum, which lies behind and below the cerebrum, is divided into two hemispheres," etc. Special care is therefore necessary to avoid the raising of false treatment hopes in the lay mind. But when we turn to such chapters in this book as "Disorders of Women and Hypnotherapy" we find the possibilities of hypnosis discussed in such varied conditions as delayed menstruation, amenorrhoea, pseudocyesis, functional uterine bleeding, dysmenorrhoea, sterility, the menopause, psychogenic leucorrhoea, pruritus vulvae, and so on. And in the field of the neuroses claims are made that hypnosis may help certain patients with anxiety states, depressions, hysterical personalities, obsessional compulsive illnesses, psychosomatic illnesses, and post-herpetic neuralgia. There are other special chapters on "Hypnosis in Midwifery" and "Hypnosis in Children." A final chapter on "Other Uses of Hypnosis" includes dentistry, obesity, smoking, homosexuality, alcoholism, and sport, and the uses of hypnosis in helping to pass examinations and as an aid to members of the theatrical profession. Few normal, neurotic, and especially hypochondriacal people will fail to find at least one of their complaints, and its treatment by hypnosis, discussed in this book. It is a conscientious and sincere attempt to discuss the possibilities of hypnotic treatment in a whole variety of conditions, and in terms understandable to the ordinary reader. But the general impression left in the lay mind, as it was in the reviewer's, may prove to be an exaggerated one as to the possibilities of hypnotherapy in so many of life's very varied ills.

WILLIAM SARGANT.

SURGICAL MANAGEMENT

Principles of General Surgical Management. By H. A. F. Dudley, F.R.C.S.E., with the assistance of B. C. Paton, M.R.C.P.E., I. F. MacLaren, F.R.C.S.E., I. B. Tait, F.R.C.S.E., and G. F. Murnaghan, F.R.C.S., F.R.C.S.E. With a foreword by John Bruce, C.B.E., T.D., F.R.C.S.E. (Pp. 203+viii; illustrated. 27s. 6d.) Edinburgh and London: E. and S. Livingstone. 1958.

This book has been written for house-surgeons, and it contains a deal of practical information set out in a most readable manner. Like some of the better books of its type, it can be read with advantage by those who are more senior. The pre- and post-operative treatment of patients is considered in a sensible manner, with particular reference to the more common complications and their prevention. There is special consideration of abdominal operations and those on the urinary tract, post-operative thrombo-embolism, and parenteral therapy. A chapter is also devoted to investigative work. The author admits to the expression of dogmatic opinion, and in a book of this kind it may well be a virtue. This book would help the surgical dresser in appreciation of his patients, and the house-surgeon who possessed its knowledge would be useful indeed. It can be strongly recommended.

E. G. MUIR.

MATURITY AND BEHAVIOUR

Physical Maturing and Behaviour at Adolescence. By J. M. Tanner, M.D., D.Sc., D.P.M. (Pp. 45; illustrated. 2s. 6d.) London: National Children's Home. 1958.

This is the 1958 National Children's Home Lecture, one of a series devoted to child welfare. It is based largely on material drawn from Dr. Tanner's book *Growth at Adolescence* (Oxford, 1955). Perhaps the only point which calls for comment is a welcome emphasis on the significance of developmental age in relation to educational achievement. The fact that children who mature early appear to be intellectually a little more advanced than those who mature late has some bearing on the reliability of a classification based on an examination at fixed age, such as the 11-plus.

T. MCKEOWN

A recent report in this *Journal* drew attention to the prevalence of tuberculosis in domestic animals. Those wishing to learn more of this subject will find it well discussed in *Tuberculosis in Animals and Man—A Study in Comparative Pathology* (Cassell and Co. Ltd., 5 gns.), by Dr. John Francis, professor of veterinary preventive medicine in the University of Queensland. About one-third of this book of 380 pages is given up to the subject of bovine tuberculosis. The next section of the book, the longest, describes tuberculosis in animals other than bovines (including wild animals), and there is a final chapter comparing the pathology and epidemiology of tuberculosis in animals and man. The book is well illustrated, and contains a list of about 600 references.

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PROGNOSIS FOR CHILDREN OF LOW BIRTH WEIGHT

The better survival rates for prematurely born infants, and particularly for those of very low birth weight, result from skilled care by experienced staff in well-equipped units. But improved survival rates do not provide ground for great satisfaction unless proof exists that the survivors live to be happy and to give happiness. Such a shrewd clinician as Sir Robert Hutchison[1] remarked almost twenty years ago : "I have a strong suspicion that, of those who survive, a large proportion turn out defective either physically or mentally." Should this prove to be so, then more efforts must be put into preventing premature births and into developing better treatment, possibly quite revolutionary treatment, for those whose premature delivery is inevitable. A bold attempt to assess the physical and intellectual development of prematurely born children was planned by the Joint Committee of the Institute of Child Health (University of London), the Society of Medical Officers of Health, and the Population Investigation Committee. All premature babies born during a single week in 1946 in England, Wales, and Scotland were matched with a control group of full-term children. The results of this survey have been published in four papers describing their health,[2] their growth,[3] their age at walking,[4] and their mental ability and school achievement at 8 years of age.[5] A higher morbidity and mortality extending beyond the first month of life existed in the premature group, the surviving members of which spent 3½ times as many days in hospital during the first two years as did the controls. Although rather shorter and lighter than the controls at 2 and 4 years, almost 40% were of normal or above normal proportions. Babies who weighed less than 4 lb. (1.8 kg.) at birth gained rather better than the others, except a group whose small size was thought to be genetic. When examined at 8 years the premature children scored slightly but significantly less than their controls at tests of reading, vocabulary, and picture interpretation, this handicap being most obvious in reading. The handicaps did not increase significantly with either falling birth weight or decreasing length of gestation. A small group emerged which was heavily handicapped in all tests and for whose low birth weight no obstetric or genetic explanation was found.

This study on prematurity began with a total of 676 matched pairs. From this, however, 177 were lost by the death of one or other member of a pair, 49 by emigration, 11 by refusal, 16 were untraced in time for testing, 8 were untested because they were educationally subnormal, and 8 because they were ill or handicapped. The final examination of mental ability was carried out on 407 pairs, or 60% of the original sample. Loss from the series of more seriously handicapped children is at least possible. J. W. B. Douglas[5] states that "in general the mental handicaps of premature children are small if we exclude those with a history of birth injury or cerebral damage." Although these clinical diagnoses are often made, paediatricians cannot always be certain that damage was sustained before, at, or after birth, and in any event such abnormality is a hazard of prematurity which must be fully taken into account when considering the fate of the prematurely born.

The immediate mortality is still much higher among infants of very low birth weight, and their progress during the first few weeks of life is more commonly interfered with by cyanotic attacks, the pulmonary syndrome, oedema, jaundice, and infection than is that of full-term infants. The mental development of this relatively small group may not be accurately reflected in the mean figures obtained from a large series of prematurely born babies. Of the premature infants studied in Edinburgh by C. M. Drillien and F. Richmond,[6] 57% were in the range 4 lb. 9 oz. (2 kg.) to 5 lb. 8 oz. (2.5 kg.), and Drillien[7] showed that among primiparous mothers 49% of infants of 38 weeks' or more gestation were premature by weight, and that among the higher parities the figure was 37%. Most of such babies were in the range 5 lb. (2.25 kg.) to 5 lb. 8 oz. (2.5 kg.). J. H. Hess and E. C. Lundeen[8] have described the progress of 82% of 259 infants who weighed from 1 lb. 10 oz. (0.75 kg.) to 2 lb. 8 oz. (1.13 kg.). They considered physical development to be average in 48% and mental development in 59%, but gave no details of the criteria of normality. Of 70 surviving

[1] Hutchison, R., *Lancet*, 1940, **2**, 799.
[2] Douglas, J. W. B., and Mogford, C., *Arch. Dis. Childh.*, 1953, **28**, 436.
[3] —— —— *Brit. med. J.*, 1953, **1**, 748.
[4] Douglas, J. W. B., *Med. Offr.*, 1956, **95**, 33.
[5] —— *Brit. med. J.*, 1956, **1**, 1210.
[6] Drillien, C. M., and Richmond, F., *Arch. Dis. Childh.*, 1957, **31**, 390.
[7] —— *J. Obstet. Gynaec. Brit. Emp.*, 1957, **64**, 161.
[8] Hess, J. H., and Lundeen, E. C., *The Premature Infant*, 1949, Philadelphia.
[9] Corner, B. D., *Bristol med.-chir. J.*, 1952, **69**, 117.
[10] Knobloch, H., Rider, R., Harper, P., and Pasamanick, B., *J. Amer. med. Ass.*, 1956, **161**, 581.
[11] Drillien, C. M., *Arch. Dis. Childh.*, 1958, **33**, 10.

babies weighing less than 3 lb. 4 oz. (1.5 kg.) at birth, B. D. Corner[9] reported that 76% were absolutely normal physically and mentally. H. Knobloch and colleagues[10] found that, out of 57 infants whose birth weight had been 3 lb. 4 oz. (1.5 kg.) or less, 44% had an abnormal condition of sufficient severity to cause concern about future development—a figure which contrasted with 8.6% for the rest of the premature infants studied and 2.6% for full-term infants.

The present studies of C. M. Drillien[11] are all the more valuable in that she has maintained almost intact a group of 75 infants weighing 3 lb. (1.36 kg.) or less at birth and has personally examined each of the survivors, some only once, but others every six months. Five died before the age of 2 years (one from bronchopneumonia), two were found dead in bed, and two died suddenly before medical assistance could be obtained. The great majority of survivors were considerably below average in both weight and height, the children being disproportionately underweight for height. Poor mental ability was distressingly common. Developmental quotients of 90 or over were found in only 37% of the pre-school group, and of the children of school age only 3 of 21 were of average intelligence. Four children omitted from the published figures have since been found to have intelligence quotients of 92, 90, 67, and 67. Only two surviving children of the original series have not been tested. No correlation was found between particular clinical disturbances in the newborn period and later mental development. Six children suffered from cerebral diplegia. Half the children had a visual defect, amounting to handicap in one-third. The incidence of respiratory infections in the first three years was four times higher than in a matched control group of full-term children. Emotional disorder was found in one-third. Mental damage was less apparent in the children of school age than in those a year or two younger. Drillien suspects that this is a result of improvement in the survival rate in recent years rather than of recovery with age, and further study of her group may supply the answer. The need for well-financed and well-planned research in this field is clear.

DELAYED AUDITORY FEEDBACK

Does the sound of a person's own voice have any effect on how he speaks? This question has been argued from a theoretical standpoint for many years. It has been suggested, for instance, that we may unconsciously control or "monitor" what we are saying by attending carefully to our utterances while we speak, and that certain abnormalities of speech may result if this process is disturbed. On this view the disorder known as jargon aphasia, in which words are strung together so as to constitute meaningless nonsense or jargon, is the result of a breakdown in the monitoring mechanism. It is assumed that, because these patients cannot understand what is said to them, they also cannot understand what they themselves are saying, and therefore they speak jargon. Against this view it has been pointed out that people with bilateral cochlear or nerve deafness, who also cannot hear what they themselves are saying, do not speak jargon, and conversely that patients who suffer from word deafness, though unable to understand what is said to them and, presumably, what they say themselves, nevertheless have normal spontaneous speech. Such arguments have previously been carried on in a climate sheltered from the cold winds of experimental proof. But the discovery in recent years of the effects of delayed auditory feedback has thrown much light on the question.

Delayed auditory feedback may be explained in the following terms. Normally while we are speaking the sound of our voice reaches the internal ears by conduction through bone and air. The speed of conduction by these two routes has been estimated by C. A. Stromsta[1] as 0.0003 second for bone conduction and 0.001 second for air conduction; normally the aerial route is by far the most important. It may be said, therefore, that we hear our own words 0.001 second after we have uttered them, and this information about the sounds we are uttering constitutes auditory feedback. This is in contrast to kinaesthetic feedback, which consists of proprioceptive information arising from the activity of the organs of speech. If this almost instantaneous auditory feedback is delayed to between 0.09 and 0.3 second, as it can be by electro-mechanical methods, curious effects are produced on the speech of normal subjects. Such a delay in auditory feedback can be achieved by recording the subject's voice through a microphone on to a magnetic tape, from which it is played back after a delay to headphones worn by the subject. In order to be effective in this way, the circuits which produce the delay in auditory feedback must permit of adequate volume and clarity in the voice as transmitted to the subject through headphones. B. S. Lee in 1950[2] and 1951[3] described the artificial stutter produced by this delay in speech feedback, and J. W.

[1] Stromsta, C. A., M.A. thesis, Ohio State University, 1951.
[2] Lee, B. S., *J. acoust. Soc. Amer.*, 1950, **22**, 824.
[3] —— *J. Speech Dis.*, 1951, **16**, 53.
[4] Black, J. W., ibid., 1951, **16**, 56.
[5] Spilka, B., ibid., 1954, **19**, 37.
[6] Beaumont, J. T., and Foss, B. M., *Brit. J. Psychol.*, 1957, **48**, 85.
[7] Spilka, B., *J. Speech Dis.*, 1954, **19**, 491.
[8] Hanley, C. N., and Tiffany, W. R., ibid., 1954, **19**, 367.
[9] Stanton, J. B., *Scot. med. J.*, 1958, **3**, 378.
[10] Cherry, E. C., Marland, P. M., and Sayers, B. McA., *Nature (Lond.)*, 1955, **176**, 874.

Black[4] found that the most effective delay period was 0.18 second.

Since this time interest in the technique has grown and several papers have appeared describing the results obtained in normal subjects. B. Spilka[5] found that when delayed auditory feedback was imposed there were increases in the average duration of syllables, the percentage phonation time, the mean vocal intensity, and in variations of vocal intensity. To these effects may be added a raising of pitch of the voice, flattening of intonation, alterations of stress and disturbance of rhythm, reduplications of consonants and syllables, and substitutions of wrong consonants, syllables, or even words. Sometimes a complete block in speech utterance occurs, resembling that found in severe stammering. J. T. Beaumont and B. M. Foss,[6] investigating individual differences in susceptibility to delayed auditory feedback, found that, while all normal subjects appear susceptible, adaptation may occur in two ways: first, if the subject speaks very slowly, and secondly if he speaks in short rapid bursts. The rapidity with which adaptation occurs appears to differ between individuals, and Beaumont and Foss conclude that people who are particularly susceptible to the effects of delayed auditory feedback may have something in common with natural stammerers. B. Spilka[7] attempted to correlate the susceptibility to auditory feedback with various personality types, and concluded that schizoid personalities are not so easily disturbed as others.

These observations show that disturbance in the time relationships between the utterance of speech and the hearing of the sounds uttered may produce a considerable disorganization in speech, and they strengthen the view that auditory monitoring plays a part in normal spoken speech. It would appear that delayed auditory feedback is a spanner which may be thrown into the workings of normal speech, disorganizing it in a predictable way. Some of the uses to which this technique may be put have been illustrated in recent publications. C. N. Hanley and W. R. Tiffany[8] have used the method for detecting psychogenic deafness and malingering. J. B. Stanton,[9] in a lecture in 1957 recently published, reviews the speech disturbances produced in normal subjects, and reports the effects of delayed auditory feedback in dysphasic patients. In this study delayed auditory feedback was used as a tool to probe the underlying physiological disturbance in the dysphasic patients. Stanton finds that, unlike the normal subjects, the patients with dysphasia do not all respond in the same manner to delayed auditory feedback. While some of the patients (those with predominantly expressive dysphasia) showed similar disturbances to those of normal subjects, the speech of others who suffered from mainly receptive dysphasia was actually improved by delayed auditory feedback. A third group with expressive or receptive speech disorders of recent onset was relatively unaffected. This use of delayed auditory feedback as an analytical tool may well lead to a more dynamic concept of the mechanisms of aphasia.

The application of delayed auditory feedback to treatment is not yet clear. E. C. Cherry and colleagues[10] have shown that many stammerers are enabled to speak normally when their auditory feedback is blocked by a loud noise. This effect of neutral noise would seem to be the explanation of the similar results obtained with delayed auditory feedback in stammerers. Possibly the reported improvement[9] in speech of patients with receptive aphasia while subjected to delayed auditory feedback may have some application to speech therapy. Finally, the results obtained with this interesting new technique also suggest that the traditional distinction between disturbances of formulation and comprehension of speech (the aphasias) and disturbances of utterance of speech (dysarthria, stammering) may be less real than had previously been supposed.

ACCURACY OF DEATH CERTIFICATES

How accurate are death certificates is a question that has been debated more often than investigated. Clearly some causes of death are easier to diagnose precisely than others, and some categories are easier to define unambiguously than others. The statistics are generally believed to be sufficiently accurate for practical use, and by grouping some categories errors can be made to cancel out. A small but interesting study of this problem, including references to previous work on it, has now been published by the Registrar-General for England and Wales.[1]

Ten large English hospitals arranged for a double death certificate to be completed on every patient dying in the hospital between February 1, 1955, and July 31, 1955. A clinician completed the first half before necropsy was carried out, and a pathologist completed the second half in the light of his post-mortem findings. In these six months 1,404 cases were accepted into the investigation from the ten hospitals, and pathologist agreed with clinician on the cause of death in 51% of them. To this figure it seems reasonable to add 28% of cases in which the disagreement between pathologist and clinician seemed to the investigators to be verbal rather than factual. In short, about 80% of these deaths were correctly certified by the clinicians.

[1] *Registrar-General's Statistical Review of England and Wales for the Year 1956*, Part 3, Commentary, 1958, H.M.S.O., 16s. 6d.
[2] Hammond, E. C., *Brit. med. J.*, 1958, **2**, 649.
[3] Paton, B. C., *Amer. J. Med.*, 1957, **23**, 761.
[4] *Brit. med. J.*, 1958, **1**, 991.

The 19% of cases in which the pathologist found fresh evidence at necropsy were chiefly among newborn babies and old people. The difficulty of identifying the exact cause of death in these groups is well known, and the figures show that the difficulty does increase throughout adulthood into old age. Agreement was highest on deaths of patients aged 15–44.

When the various causes of death were considered to see which groups evoked most agreement or disagreement, some striking figures were obtained for cancer of the lung, which was notably under-diagnosed, especially in old patients. Of 87 cases assigned to this cause 8 were found at necropsy to have another cause, and in 30% of the remainder the pathologist found a previously unsuspected cancer of lung or bronchus. Though the doctors who took part in this investigation are not put forward as a representative sample of the profession (they were all members of hospital staffs, for instance), their results suggest that the much higher death rate from lung cancer in Great Britain than in the U.S.A. cannot be attributed to over-reporting of it here, as has recently been conjectured.[2] Arteriosclerotic and coronary heart disease was another group that caused disagreement, for on 227 certificates clinician and pathologist agreed in only 41%. This agrees closely with the figure of 44% accuracy rate for myocardial infarction found by B. C. Paton[3] in a review of necropsies at the Edinburgh Royal Infirmary, discussed recently in these columns.[4] In the Registrar-General's investigation a particularly notable cause of death which clinicians mistook for coronary disease was pulmonary embolism.

While disagreement about facts was prominent in the diagnosis of coronary disease, disagreement about words largely confused the diagnoses of death from hypertensive disease. Among 86 cases in which this was given as the diagnosis, disagreement between clinician and pathologist was noted in 66 cases (77%). But in 52 of these cases (60%) wording was the cause of difference. This is a natural consequence of the association apt to be found between hypertension and renal or cerebrovascular disease.

TREATMENT OF CARBON MONOXIDE POISONING

An important communication from the Medical Research Council on the use of carbon dioxide in the treatment of carbon monoxide poisoning appears at p. 1408 of the *Journal* this week. After studying the results of some recent experiments by the M.R.C.'s Breathing Apparatus Committee, and of data obtained from independent work on human volunteers, the M.R.C. concludes that "the administration of a mixture of carbon dioxide in oxygen leads to the more rapid elimination of carbon monoxide from the blood than does the administration of oxygen alone."

Three years ago a committee of the M.R.C. considered the problem of whether or not carbon dioxide should be given with the oxygen as a first-aid measure to patients poisoned by carbon monoxide, and recommended that it should not be.[5] The reasons for this decision were fully set out and are complex, but an important one was that, in the uncontrolled conditions of first aid, carbon dioxide might accumulate dangerously in the patient's tissues. Dr. H. L. Marriott[6] challenged the committee's conclusion, because he considered, as others have done, that the administration of oxygen and carbon dioxide stimulates the depressed breathing of patients severely gassed with carbon monoxide. It is this view that the M.R.C. endorses in its latest statement.

Though the difference in the results obtained by the two methods of treatment may be small—and none was found in an analysis of some admittedly imperfect statistics[7]—clearly nothing short of the very best is good enough for patients hovering between life and death, as these usually are. And, so far as it can be ascertained, the best treatment does seem to be a mixture of 5% carbon dioxide with 95% oxygen when the patient is suffering from carbon monoxide poisoning. For the treatment of other types of asphyxia and anoxia the M.R.C. continues to advocate pure oxygen.

EPIDEMIC NEPHRITIS

The typing of *Streptococcus pyogenes* has been used for many years as a useful epidemiological device for determining the origin of outbreaks of streptococcal disease and in studies of the spread of streptococcal infection in communities. The type of organism found may also have clinical significance. It has been noticed that certain types, and particularly type 12, are more often associated with the development of nephritis than others. In 1954 M. J. Wilmers, A. C. Cunliffe, and R. E. O. Williams[8] found that of 31 strains of *Streptococcus pyogenes* recovered from cases of acute glomerulonephritis 28 were of type 12. This is taken a stage further by two articles appearing in this issue. Dr. J. T. A. George and his colleagues describe the finding of four cases of acute nephritis among 24 boys in a residential school who had suffered from acute pharyngitis 10 to 19 days previously. About two months after the sore throats had occurred seven of the boys were still harbouring *Streptococcus pyogenes* type 12, and at this stage red cells were found in the urine of five children not previously suspected of having nephritis. Investigations carried out in neighbouring schools showed type 12 or related strains to be present in some of them; red-blood cells and casts were found in some specimens of urine, but only in the infected schools. Nearly a year later, when there were signs that further cases of nephritis were occurring, letters were sent to all doctors practising in York and the

[2] Donald, K. W., and Paton, W. D. M., *Brit. med. J.*, 1955, 1, 313.
[3] Marriott, H. L., ibid., 1955, 1, 664.
[4] Hill, A. B., ibid., 1956, 2, 1220.
[5] Wilmers, M. J., Cunliffe, A. C., and Williams, R. E. O., *Lancet*, 1954, 2, 17.
[6] *Report of Ministry of Health for the Year 1957*, Part 2, p. 42. H.M.S.O., 1958.

North Riding. This brought to light 48 cases. In spite of the fact that many of them were not examined bacteriologically until some time after onset of the infection, type 12 streptococci were recovered from a substantial proportion of them. The disease was found most commonly in children of school age, and this was the finding also in the other survey reported by Drs. M. J. Pleydell and W. J. A. Hall-Turner from Northamptonshire. Here investigation of the circumstances of a small outbreak of nephritis in a village school suggested that the disease might be more widespread. Again all doctors practising in the county were circularized by the medical officer of health and asked to report any cases under their care. As a result 89 cases of nephritis, occurring over a period of three years, were brought to notice, and type 12 streptococci were recovered from a high percentage of the cases.

In both these investigations information on the local distribution of nephritis was obtained by asking doctors in the locality to notify cases, and this method was successful in demonstrating the distribution of the disease in the area. Whether such a procedure should be adopted more generally may depend partly on the use that can be made of the information so obtained. It has been suggested that the existence of a case of acute nephritis may justify the use of energetic preventive measures against the spread of streptococcal infection, including the giving of prophylactic penicillin to close contacts.[9] Pleydell and Hall-Turner mention the advisability of protecting nephritic children from reinfection: one way of doing this would be to exclude them from school when upper respiratory infections were present.

MEDICAL SERVICES REVIEW COMMITTEE

The first meeting of the Medical Services Review Committee, sponsored by the Royal Colleges, the Scottish Royal Corporations, the College of General Practitioners, the Society of Medical Officers of Health, and the British Medical Association, was held on November 27. Sir Arthur Porritt, the chairman, presided, and the following have been appointed as members of the committee: Dr. T. Anderson; Dr. W. Ferguson Anderson; Dr. J. T. Baldwin; Dr. I. R. C. Batchelor; Sir Harold Boldero; Mr. W. S. Braidwood; Mr. R. Brearley; Professor J. Bruce, P.R.C.S.Ed.; Dr. H. D. Chalke; Professor A. M. Claye, P.R.C.O.G.; Mr. E. Cope; Dr. A. B. Davies; Dr. T. B. S. Dick; Miss A. M. Dickins; Dr. J. Fry; Dr. A. Rae Gilchrist, P.R.C.P.Ed.; Dr. I. D. Grant; Dr. C. F. Hawkins; Mr. W. Hawksworth; Mr. R. G. Henderson; Dr. J. H. Hunt; Mr. Arthur Jacobs, P.R.F.P.S.; Dr. A. M. Maiden; Mr. D. F. E. Nash; Dr. I. Rannie; Dr. T. Ferguson Rodger; Dr. J. M. Rogan; Mr. J. A. Ross; Sir James Paterson Ross, P.R.C.S.; Mr. T. Holmes Sellors; Dr. G. Swift; Sir Tudor Thomas; Dr. J. B. Tilley; Dr. F. G. Tomlins; Dr. S. Wand; Professor R. C. Wofinden. The committee's terms of reference are to review the provision of medical services to the public, and their organization, in the light of ten years' experience of the National Health Service, and to make recommendations.

RE-STENOSIS OF THE MITRAL VALVE

The surgical treatment of mitral stenosis has now been practised for a decade,[1] and with the publication from various centres of reports on patients observed for five years or more the early results of this operation can be assessed. A disappointing outcome in some cases is re-stenosis of the mitral valve, and in a recent article J. R. Belcher[2] discusses this eventuality. It is too early yet for accurate figures to be obtainable, but a re-stenosis rate of between 2 and 5% is usually quoted. Glover and his colleagues,[3] among others, believe that if complete division of both fused commissures has been done at the first operation re-stenosis will not occur: they have not found a case in their own series. Most authors agree that there are two main groups of patients with mitral valve disease who may need a second operation. The first and larger is that described by Belcher as "false re-stenosis," believed to be the result of an inadequate first operation. This may be due to the surgeon's inexperience, and is consequently higher in the earlier cases of his series, but it may also be due to pathological changes such as gross calcification in the valve. It will be interesting to see whether improved surgical techniques in mitral valve surgery, such as C. P. Bailey's[4] right-sided approach or the transventricular dilatation advocated by A. Logan,[5] will lower the incidence of re-stenosis in the next few years. Since a rigid valve is more likely to give trouble, division of both commissures, if at all possible beyond R. C. Brock's[6] critical area of tendon insertion, should restore the valve to maximum mobility and reduce the chances of re-stenosis. Coincident with commissural fusion is the matting together of chordae tendineae below the valve, and the surgeon must ensure that they are separated at operation. Some suggest that if a satisfactory opening of 2½ to 3 fingerbreadths can be obtained by splitting the anterolateral commissure alone the posterior commissure can be left, unless it splits easily. This may reduce the operative mortality, but may also lead to a higher recurrence rate. Belcher found that in his series no second operation was needed in 186 patients who had had good commissural division; but out of 43 patients at whose operations the split was classified as fair five needed second operations, while out of eleven patients with a poor split six had to be operated on again.

Cases of true re-stenosis of the valve after a satisfactory first operation form the second main group, though a much smaller one than those with false

[1] Bailey, C. P., *Dis. Chest*, 1949, **15**, 377.
[2] Belcher, J. R., *Brit. Heart J.*, 1958, **20**, 76.
[3] Glover, R. P., Davila, J. C., O'Neill, T. J. E., and Janton, O. H., *Circulation*, 1955, **11**, 14.
[4] Bailey, C. P., Bolton, H. E., and Morse, D. P., *Surg. Clin. N. Amer.*, 1956, **36**, 931.
[5] Logan, A., quoted by Belcher, J. R.[2]
[6] Brock, R. C., *Brit. Heart J.*, 1952, **14**, 489.
[7] Magarey, F. R., *Brit. med. J.*, 1951, **1**, 856.
[8] Soulié, P., Joly, F., Carlotti, J., and Servelle, M., *Amer. Heart J.*, 1957, **54**, 695.
[9] Bywaters, E. G. L., Hallidie-Smith, K., and Thomas, G. T., *Brit. med. J.*, 1957, **1**, 1234.

re-stenosis. The cause of this is not certain, but continued rheumatic activity or an attack of subacute bacterial endocarditis is usually blamed. It is not clear how an avascular valve can lay down further fibrous tissue, but F. R. Magarey[7] has suggested that a platelet and fibrin thrombus forms between the roughened edges, so sticking them together. It is difficult to be certain of the occurrence of true re-stenosis unless the same surgeon does both operations and has accurate records of the state of the valve, or unless the valve can be inspected at necropsy. Ideally, simultaneous estimations of pressure gradients across the mitral valve and of the cardiac output before and after each operation are the only sure way of supporting the evidence of the surgeon's finger *in vivo*. F. Soulié and colleagues[8] noted that the second operation was always harder owing to increased rigidity and thickening of the valve leaflets and that instrumental dilatation was always needed. In spite of a satisfactory original operation, true re-stenosis may be expected to occur in from 2 to 5% of cases.

E. G. L. Bywaters and his co-workers[9] recommend the prevention of further attacks of rheumatic fever in children by long courses of antibiotics, and in the United States it is common practice to give penicillin for long periods to patients who have had a mitral valvotomy. The administration of antibiotics might therefore be one possible way of reducing the incidence of re-stenosis. Before a second operation for stenosis of the mitral valve is performed the degree of damage to the myocardium by the rheumatic process, the amount of mitral incompetence present, and the height of the pulmonary vascular resistance should all be assessed, since any of these may be responsible for a poor post-operative result. Operation can only relieve valvular obstruction if proved to be present, and, if successful, it may lessen the severity of these other defects.

FOOTBALL AND THE HEART

The problem of preventing coronary arterial disease is of central importance in cardiology to-day. So far we have only faint clues to its solution, important among these being the effect of diet on the healthy state of the coronary arterial tree, and occupational and possibly racial factors.

Whether exercise, or lack of it, is a factor in the causation of the disease is also an important consideration. Recently William C. Pomeroy and Paul D. White[1] investigated a group of 355 men who had distinguished themselves athletically at football while at Harvard University between the years 1901 and 1930. Coronary arterial disease as a cause of death was only slightly less frequent among this group of athletes than in all adult white males in the State of Massachusetts in the year 1940, chosen arbitrarily as a comparison. More accurate comparison with Harvard graduates of the same age who had not played football was desirable, but the necessary data were not available. Interesting differences, however, were observed within the group of athletes. One was the higher incidence of "unfavourable family health," which usually meant coronary arterial disease, in the relatives of those athletes developing coronary disease themselves in later life. Another interesting finding was that no member of the group of athletes developed coronary arterial disease who continued to take active and strenuous exercise throughout the rest of his life after leaving the university. It might be supposed that this was a reflection of their good health rather than the cause of it, but against this was the fact that in most cases the habit of active exercise, or abandonment of it, was formed quite early in life, before the onset of the first symptoms of coronary arterial disease. No very significant differences in other factors investigated were noted between those athletes who did, or did not, develop disease of the coronary arteries: these included consumption of alcohol, smoking, diet (about which data were inadequate), and body build. More work is needed to determine the significance of these findings in this small group of athletes, but the tentative conclusion from this study is that an athlete who continues to take active exercise throughout his life is unlikely to develop coronary arterial disease.

[1] Pomeroy, W. C., and White, P. D., *J. Amer. med. Ass.*, 1958, **167**, 711.

RICHARD BRIGHT, 1789–1858

"Richard Bright was an extraordinary man. It is impossible to place geniuses in order, but he would certainly be among the first five or six in our profession." This is what Sir William Hale-White wrote in the *Guy's Hospital Reports* thirty-seven years ago. This article is now reprinted in a special number of this most notable among hospital periodicals, middle in age between the *Lancet* and the *B.M.J.*, as Dr. E. R. Boland told us at a commemorative dinner given by Guy's Hospital Medical School on Monday in the Royal College of Physicians, where Bright was admitted as a Licentiate in 1816 and as a Fellow in 1832. An Englishman who qualified in Edinburgh in 1813, Richard Bright's association with Guy's began as early as 1811. In 1820 he was elected assistant physician to the hospital, and in 1824 full physician. He died on December 16, 1858. It was his "Reports of Medical Cases" in 1827, in which albuminuria and dropsy were causally linked with pathological changes in the kidney, that gave him his fitting place in the history of medicine, and two long papers on what has since been commonly known as "Bright's disease" appeared in 1836 in the first volume of *Guy's Hospital Reports*, the current number of which, in its gold and blue cover, completes the 107th volume with an act of filial piety that will be a delight to all and a collector's piece for the medical historian. We learn from it that when he was 24 Bright wrote to his father, "You must know that surgery is at this moment rising very fast at the expense of medicine—and we must do our best to keep our ground." One of the signs that surgery is still rising very fast is the fact that the editor of this special number dedicated to Richard Bright is a surgeon, Sir Russell Brock.

Drug Treatment of Disease

DRUG TREATMENT OF NEURITIS

BY

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Neuritis is a much misused term. Many of the conditions to which it is sometimes applied are in fact of mechanical origin. For instance, brachial neuritis may be used as a diagnostic label for pain in the arm accompanied by paraesthesiae and neurological signs when in fact the basic cause is compression or irritation of posterior roots by a protruding intervertebral disk or cervical spondylosis, pressure on the brachial plexus by a cervical rib or by drooping of the shoulder girdle in the axillary-inlet syndrome, or injury of a peripheral nerve, as by compression of the median nerve in the carpal tunnel or friction to the ulnar nerve at the elbow in association with cubitus valgus or osteoarthritis of the elbow. Similarly, in the lower limb, sciatic neuritis and femoral neuritis probably do not exist, the majority of cases of sciatica and anterior crural pain being due to mechanical causes, such as protrusion of intervertebral disk or other lesions compressing the nerves or posterior roots. In such cases drug treatment can only be of very limited value and consists of suitable analgesics. The essential treatment for the condition—immobilization, physiotherapy of various types, manipulation, or surgical treatment—varies with the aetiology. The administration of vitamin-B preparations for such conditions has no rational place in treatment.

Multiple peripheral neuritis or polyneuritis is to some extent also a misnomer, but in many of such cases there are changes in the parenchyma of the peripheral nerves. There are many possible causes of polyneuritis, and in some of them drug treatment is of value.

Deficiency of Vitamin B_1

Deficiency of aneurine (vitamin B_1) in relation to the carbohydrate intake may cause peripheral neuritis as a result of disturbance of carbohydrate metabolism in the nervous system at the pyruvate stage. In such cases the amount of pyruvate in the blood is increased, and this can, if necessary, be shown by a pyruvate tolerance curve. Actual deficiency of aneurine in the diet is rare in the United Kingdom, but defective absorption may occur in cases of steatorrhoea, long-continued diarrhoea, extensive resection of the small intestine, and long-continued fever; and a deficiency peripheral neuritis may occur in these conditions. The peripheral neuritis of alcoholism is to a large extent due to aneurine deficiency in relation to the carbohydrate intake.

In such cases treatment should be started at the earliest opportunity before degenerative changes have occurred in the peripheral nerves and when the lesion is still a biochemical one. The first essential is large doses of aneurine by injection, and, as in many cases there is also a deficiency of other elements of the vitamin-B complex, and of vitamin C, these should be given in addition, together with a normal diet. A suitable preparation for starting treatment is "parentrovite" high potency intramuscular injection, each injection of 7 ml. containing aneurine hydrochloride 250 mg., nicotinamide 160 mg., riboflavin 4 mg., pyridoxine 50 mg., and ascorbic acid 500 mg. After daily injections have been given for a week oral treatment should be continued with tab. aneurin. co. fort. (*B.N.F.*), which contains aneurine hydrochloride 5 mg., riboflavin 2 mg., nicotinamide 20 mg., and pyridoxine 2 mg., a tablet being taken four times a day.

Acute Infectious, Toxic, or Febrile Polyneuritis (Guillain–Barré Syndrome)

Although the aetiology of this type of polyneuritis is uncertain, the evidence suggests that it may be allergic in nature. For this reason it has been treated with cortisone or prednisone. The natural history of the disease is for rapid deterioration to take place over the course of a few days up to two to three weeks; if the patient survives the acute stage, rapid recovery of function usually occurs. This type of natural history makes it difficult to estimate the value of cortisone therapy, but published cases and personal experience certainly suggest that it is of value in stopping deterioration and possibly in hastening recovery. Cortisone should be given as early as possible, and a suitable dosage for an adult is 300 mg. (in divided doses) daily for two days, 200 mg. for two days, and then 100 mg. daily for ten days, the dosage then being gradually tailed off. Prednisone is less likely to cause retention of salt, and for this reason is usually the preferable preparation to give (5 mg. of prednisone being equivalent to 25 mg. of cortisone).

Lead "Neuritis"

This condition is probably the result of a disturbance of resynthesis of phosphocreatine in the muscles affected rather than a disorder of the peripheral nerves. In the last few years the treatment of acute lead-poisoning, such as lead encephalopathy, has been greatly improved by the introduction of the chelating agent calcium disodium ethylenediamine tetra-acetic acid, or sodium calciumedetate ("calcium disodium versenate"), and though reports of its use in lead "neuritis" are scanty it would seem to be the rational method of removing the lead from the body in this condition. When this chelate is administered to a patient with lead-poisoning, the lead replaces calcium in the chelate, the resulting compound being excreted in the urine. The chelated lead compound does not ionize and so there is little danger of causing symptoms of acute lead-poisoning, which was always a risk with the older methods of removing lead from the body.

The preparation is supplied in 5-ml. ampoules containing 1 g. in a 20% aqueous solution; this should be diluted in 250–500 ml. of injection of sodium chloride *B.P.* or injection of dextrose *B.P.* and administered by intravenous drip over the course of an hour. For adults this dose should be given twice daily for five days; then there should be a rest for two days, followed by a further five days of treatment. Calcium disodium versenate can be given by mouth, but it is not yet clear how effective this method of administration is in removing lead from the body.

Diabetic Neuritis

The most essential treatment in the peripheral neuritis associated with diabetes mellitus is the adequate control of the disease by diet and in most cases insulin. Patients suffering much pain may sometimes have this alleviated by injections of vitamin B_{12}, a suitable dose being 1,000 μg. daily for a week. In the minority of cases where there is burning pain in the feet, calcium pantothenate 50 mg. three times a day by mouth is sometimes helpful.

Other Types of Polyneuritis

In the rare cases of polyneuritis due to ingestion of arsenic, dimercaprol (B.A.L.) is the best treatment. This

substance forms a stable compound with arsenic, not only preventing arsenic from combining with tissue proteins but also causing existing arsenic-protein complexes to dissociate. B.A.L. is available in 2-ml. ampoules, each containing 100 mg. of the substance. It should be administered by deep intramuscular injection, in an adult 100 mg. being given four times in the first twenty-four hours, twice daily on the second, third, and fourth days, and once daily for two further days. Local pain may follow the injection, and intramuscular abscesses have been reported. With this dosage toxic symptoms are not likely, but vomiting, headache, generalized muscle pain, and paraesthesiae in the limbs have at times been recorded. B.A.L. is occasionally beneficial in cases of polyneuritis associated with treatment by gold and bismuth compounds. It has also been tried in cases of chronic polyneuritis of uncertain aetiology, but the results have been disappointing and there does not seem to be any real justification for its use here.

When polyneuritis is due to periarteritis nodosa it may respond to cortisone or prednisone; but when it is due to such systemic diseases as carcinoma of the bronchus, porphyria, and primary amyloidosis drug treatment has no appreciable effect on the neurological conditions.

Treatment Apart From Drugs

Administration of drugs plays only a minor part in the treatment of most cases of polyneuritis other than those associated with deficiency of aneurine, absorption of lead or arsenic, and, to a lesser extent, acute polyneuritis of toxic or infective origin. The main essentials of treatment are bed rest in the acute cases, in which tachycardia frequently occurs, measures to deal with bulbar palsy and paralysis of the respiratory muscles, and physiotherapy. When the bulbar nerves are affected, postural drainage, pharyngeal suction, physiotherapy to the chest, and feeding through a gastric tube are essential, and in some cases tracheotomy with positive-pressure respiration is necessary to enable the patient to get through the acute phase of the disease. In patients with intercostal and diaphragm paralysis without bulbar paralysis a box or cuirass type of respirator may be useful, but if there is in addition bulbar paralysis positive-pressure respiration will be essential. The object of physiotherapy is to prevent contractures and stiffness of the joints by passive movements and light splintage. When the acute phase is passed active movements, including movements against resistance but within the limits of muscle fatigue, are helpful to the patient.

SEXUAL OFFENCES AS SEEN BY A WOMAN POLICE SURGEON

BY

NESTA H. WELLS, M.B., Ch.B.
Surgeon, Manchester City Police, 1927–54

The Wolfenden Report has brought homosexuality and prostitution into the headlines, but the discussion of sexual misbehaviour has not usually arisen. The general public do not appreciate how much is going on all around us all the time, nor do they realize how much education and research is needed if these offenders are to be given adequate and proper treatment.

Many cases are not reported to the police for various reasons, including the reluctance of the parents to let the child be seen by the male police surgeon after being assaulted by a man, and their dislike of the publicity of a court case. Having lived in the poorer parts of Manchester, Councillor Annie Lee (before becoming an alderman) knew the conditions there and how people felt, and when she became a member of the Manchester Watch Committee she managed to persuade them in 1927 to appoint a woman police surgeon for the special purpose of examining, when required, any women and children seen by the police.

This was a pioneer step, and from the letters I received when appointed it seemed to be the first of its kind, not only in Britain but anywhere else. Apart from London, very few towns, if any, have as yet made similar appointments. As Manchester is probably little different from other cities, I hope that the following survey may help to show the need for the examinations to be done by a woman and also the need for the consideration of various other points in connexion with sexual offences.

Present Survey

My figures concern only those cases which were referred to me by the police for examination during the years 1927 to 1954, when I retired. They do not of course include cases needing no medical examination, such as "indecent exposure," which during 1950–4 averaged between 280 and 330 a year. Nor do they compare easily with figures given in the Chief Constable's Reports for the various crimes. For instance, in 1952, there were:

Indecent assault cases known to police	109
" " " cleared up	93
Total number proceeded against	56
Referred to higher court (included above) ..	7
Complainants seen by me	51

The differences arise in various ways. A number of offences are only technically indecent assault and do not need a medical examination. One man may have attacked more than one child, so that my figures will be increased in comparison with the number of the criminals. Actually 19 cases detected by the police in 1952 were committed by only four men. In quite a number that I saw, the men had got away and could not be traced, though occasionally they were found after attacking another child. In cases where I had found nothing these might go to court if there was other corroborative evidence or the men admitted the offence.

My figures must therefore be regarded as cases of "suspected offences" needing medical examination. The findings were often not very helpful: at times they were consistent with but not necessarily the result of interference; at times they gave definite corroboration to the story. However, no attempt has been made to analyse these results, but to give a picture of the kind of case which needed to be seen, the ages of the children involved, and some of the problems that arise.

Fig. 1 shows the increase in the total cases seen each year from 1927 up to 1939, followed during the early war years by a marked drop. After the war, however, the numbers rose again, reaching a higher level than ever before. The graph also shows the number of cases of indecent assault, carnal knowledge, and incest seen. Rape, common assault, and miscellaneous cases kept fairly level, at between 0 and 10 each, over the whole period until 1954.

A survey to July, 1937, after my first 10 years, showed an increasing number of cases seen; there were as many during the last four years as during the first six years. The remaining 17 years have been divided into four groups—the three

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pre-war years, the five war years, and the two five-year periods since. The total came to just under 2,000 cases, with the average annual figure for each period rising from 48 to 86 in the pre-war periods, dropping during the war to 64, followed by a marked rise since the war to 92 in the last five-year period. The averages for the individual offences are shown in Fig. 2.

Table I gives the offences since 1937, arranged according to the age of the complainant, and Fig. 3 puts them in graph form. It will be seen that 82% of the subjects were under 16 years—the age of consent. Of these, 26% were 13–15 years old, thus leaving over half aged 12 and under. The

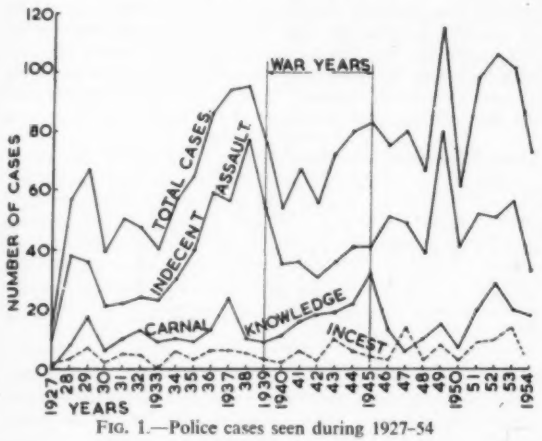


FIG. 1.—Police cases seen during 1927–54

most striking thing of all is that, of these 822 young girls, well over half were 7 years or under, and 254 were only 5 or 6 years old.

It will also be seen that nearly 20% of all cases were 5 years or under, and 34% were 7 or under, a point which is referred to later. Fig. 3 also shows that the indecent assault cases mainly involve those under 11 years, the carnal knowledge cases those from 14 to 16, followed by a spike for rape, assault, and incest cases between 20 and 30. Otherwise a fairly even scatter from 0 to 10 cases is seen in most ages.

Suspected Indecent Assault

These cases always form the largest proportion of all those seen, varying from 45% to 80%, but usually they were between 55% and 65%. The increase during the first 10 years had been very marked, and it continued to a peak in 1938, but with the outbreak of war in 1939 the picture changed completely. The indecent assault cases dropped and the carnal knowledge cases rose.

Possible reasons for this drop would include the evacuation from the city of some of the children in the early war years, with perhaps a lower child population following the lower birth rate in the 1930's. Then also the men left at home were more fully occupied, working long hours, there were fewer loafers about, and the blackout kept people more at home. But, whatever the causes, the number dropped by nearly one-half, from an average of about 62 a year for 1937–9 to 35 a year for 1940–4 (see Fig. 2). Unfortunately they have risen again, as have all the sexual offences, to 52 and 49 a year respectively, for the last two post-war periods.

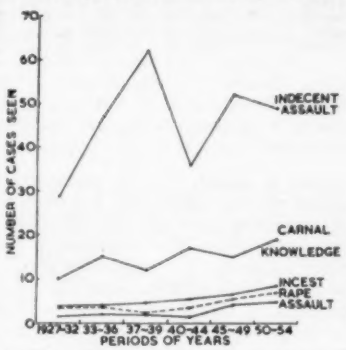


FIG. 2.—Annual average number of each offence in each period of years.

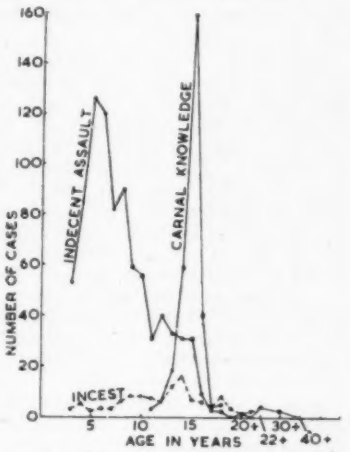


FIG. 3.—Totals of types of cases by age. 1937–54

Indecent assault was the principal reason for seeing the younger children, and, as has already been said, half the subjects were under 7 years, with many more aged 5 and 6 than any other age. Even the very tiny infants of 3 years and under were more numerous than the 9- and 10-year-olds. Table II shows that the age distribution is very much the same in each of the periods, though the actual figures vary. The highest annual numbers seen were in 1938 and 1949, when they were 78 and 80 respectively, and the lowest figures were during 1930–3 and the war years, lying between 20 and 40 a year. The variation occurred mainly in those under 9 years.

With so many young children involved a difficult situation often arises, as most courts consider that a child under 7

TABLE I.—*Total Cases of each Offence, 1937 to 1954, According to Age of Complainant*

Age:	3–	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22+	30+	40+	50+	60+	Total
Indecent assault ..	53	85	126	120	82	90	59	56	31	40	33	31	31	9	3	2	0	1	0	4	2	0	0	0	858
Carnal knowledge ..	0	0	0	0	0	0	0	0	3	6	18	59	159	40	4	5	0	0	0	0	0	0	0	0	294*
Incest	3	5	2	3	3	6	8	8	7	6	12	16	7	6	4	8	3	1	2	4	0	0	0	0	114†
Rape	0	0	0	0	0	0	0	0	0	0	0	0	4	5	9	9	5	11	2	21	13	8	2	3	92
Assault	5	0	0	1	0	1	1	0	1	2	1	2	3	1	5	3	1	3	3	14	7	2	1	1	58
Miscellaneous ..	3	0	0	2	1	0	3	0	0	0	0	0	0	1	1	0	1	1	2	4	7	4	0	0	92
Total	64	90	128	126	86	97	71	64	42	54	64	108	204	62	26	27	10	17	9	47	29	14	3	4	1,446
	282 (19·6%)			540 (37·5%)							376 (26%)			142 (9·8%)					106 (7·3%)					
Jan. 1937 to Sept. 1954	494 (34·1%)			1,198 (82·8%)										(248 17·2%)										1,446
Aug. 1927 to July 1937	88 (15·4%)			446 (78·2%)										124 (21·7%)										570

* 70 Pregnant. † 37 Carnal knowledge.

	2,016
Deduct 7 months overlap in 1937	57
Total cases seen	1,959

TABLE II.—*Indecent Assault Cases at various Ages Grouped in Periods 1937–54*

Ages:	3–	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22+	30+	40+	Total	Yearly Av.
1937–9	9	20	32	22	17	26	13	8	10	11	8	2	5	1				1		1			186	62
1940–4	15	13	23	22	16	18	14	13	4	9	9	9	7	2	0	1				2	2		179	35·8
1945–9	16	24	39	43	28	28	18	17	5	11	7	10	9	3	1					1			260	52
1950–4* ..	13	28	32	33	21	18	14	18	12	9	9	10	10	3	2	1							233	49
Total for 1937–54																							858	48·3
,, ,, 1927–32																							173	28·8 p.a.
,, ,, 1933–6																							188	47 p.a.

* Total period of four years and nine months.

cannot be sworn. "The unsworn evidence of a child of tender years is admissable, *but* when this is given on behalf of the prosecution the accused shall *not* be liable to be convicted *unless* that evidence is corroborated by some other evidence . . . implicating him." It is allowable to accept as such evidence what was said in way of complaint, provided it was made at "the earliest possible moment." In many cases, however, one cannot use this complaint because there was delay, perhaps because the child did not know the first person met, or the man may have threatened her if she told anyone. As the man is unlikely to assault the child where he can be seen, the case often falls through lack of corroboration.

Difficulty has also arisen where the witness of an offence has been a child under 7 and the unsworn evidence has been disallowed, although the child made a good statement and had obviously been telling the truth. Unless the man admits the offence the case may not be taken to court or it may be dismissed. One bad case concerned a man who kept a shop and bribed little girls into the back room by giving sweets or pennies. He usually took one or two at a time, but it went on for some considerable period, so that, although five or six girls were involved, the statement of each was corroborated by one or more other children. The man was defended in the police court, and he elected to be tried by a jury; but when the case went on to the Sessions the Recorder turned it down, without hearing, because there was no sworn evidence, all the girls being under 7 years, and no complaint had been made.

This problem needs very careful consideration, among others concerning children's evidence in general. One must respect the rights of the individual, but it should not always have to be those of the accused that are respected and those of the injured that are ignored.

Suspected Carnal Knowledge

Apart from the initial rise in the first period after my appointment (Fig. 1) the numbers for carnal knowledge remained fairly steady at about 10 to 14, with the exception of 1937, up to the early war years. After 1940, however, we had many of the Forces of our own and other countries stationed in and around Manchester, and there were always many of them to be found wandering about the city streets. They were met by many young women, including the 14- to 16-year-old girls, with the result that the carnal knowledge cases increased and reached a peak of 32 in 1945. After the end of the war the figure fell to almost pre-war level, but as people settled into peacetime life in the 1950's with greater freedoms, so also did the carnal knowledge cases rise again to 29 in 1952, with an average of nearly 20 cases a year in the last five-year period. They also formed a higher percentage of all the cases seen during the last few years (Fig. 2).

As one would expect, the largest number of cases are found in the 15-year-old group (Table I and Fig. 3). A comparison of the numbers seen in each period of years is given in Table III, in which the increase in the 1950–4 period is clearly shown.

For carnal knowledge it is only necessary to prove penetration with the penis if the girl is under 16 years, as it is an offence whether she gives consent or not. What the graphs cannot show was the change in the type of case history which developed during and after the war. Previously there were not only fewer cases but in most of them the girl was not a willing partner and had been taken advantage of, possibly because she had been a bit slow in the uptake. But during the war almost all the girls had been going out with members of the Forces or deliberately meeting them in town or near the camps. They were seldom found after the first offence, and, as many of the men were known to the girls only as Charlie or Johnny, etc., it was often impossible to track them and take steps against them. These girls therefore were being seen more as being "in moral danger" or "in need of care and protection" than as ordinary police cases.

TABLE III.—*Carnal Knowledge Cases, Giving Ages in Groups of Years*, 1937–54

Ages:	11	12	13	14	15	16	17	18+	Total	Yearly Average
1937–9	0	2	3	11	16	4	1	1	38	12
1940–4	0	3	7	15	48	10	1	2	86	17
1945–9	1	0	3	13	42	16	1	0	76	15
1950–4	2	1	5	20	53	10	1	2	94	19
Total	3	6	18	59	159	40	4	5	294	16·6

The voluntary homes run by the various religious denominations to which these girls had to be sent were soon full to overflowing, so the Home Office had to open more remand homes and approved schools in 1942 and 1943. The remand home in Manchester, to which I was appointed as M.O., was fortunately equipped for the treatment of venereal disease, and most of these girls needed such treatment. However, the majority of them went direct from the courts for medical reports and therefore are not included in this survey. Their background was nearly always a broken home of some kind or bad parental influence or example, and their I.Q.s lay on the low side of normal, usually between 70 and 90, though there were some of 60 and under.

The men concerned were for the most part the poorer type of the average man in the Forces, who may have thought that by going with a young girl he might avoid V.D., etc.; but as he was not always the first, he might catch infection which she had acquired from an earlier partner.

The carnal knowledge cases involving girls of 11 and 12 years were mostly those of boys under 16 years. Where girls of 16, and therefore over the age of consent, were concerned, they were either suspected to be pregnant or the history suggested that intercourse had taken place before the age of 16. Over the period 1937–54 there were 70 who were pregnant, about 23% of the cases of carnal knowledge seen. Those girls who were 17 years or over were very mentally slow or known to be defective, and should therefore have had some protection in law; but if they went to court this never seemed to apply. That is one of the points which should have further investigation.

There were also cases of procuration by proprietors of immoral houses, perhaps sending out young girls to be picked up by car kerb-crawlers. Some of these and the remand-home type of girl, even after an approved-school training, may revert to the "streets" and the easy money obtained there, and their treatment is a hard problem. It would be easier if people would believe that extramarital intercourse was wrong and promiscuousness in men was not accepted as a normal occurrence. If there was no demand

for females the supply would go down. It is therefore necessary to raise the moral standard of the community as well as make the laws applicable equally to men and women.

Suspected Incest Cases

Included in these figures are those of indecent assault by relatives (see Figs. 1, 2, and 3). One to three of the five cases seen each year would be true incest with penetration by the penis; and here again since the war the numbers went up to 6.5 a year for the 1945–9 period and to 8.6 a year for 1950–4. Of the total 114 cases, 37 showed penetration (see Table I). The age distribution is also given, 14 years being the most frequent time.

In the majority of cases the father had assaulted the daughter, but in some the offence had been between brother and sister. Where the girl was over 16 years, the men seemed to have taken advantage of the fact that she was a bit mentally slow and more easily intimidated.

Suspected Rape Cases

A similar kind of picture is seen here, with a steady number of 2.2 to 3.8 a year in each of the earlier periods, and a definite rise after the war to 5.6 and 7.1 a year respectively for the last two periods (Fig. 2). Police records for the city show that on only one occasion since 1927 did figures for rape reach 10, and that was in 1950. Table I gives the numbers seen in each age group.

Before the war there were fewer suspected cases, and most of them were genuine, though not always proved to the satisfaction of the court. One of my earlier cases fell through because the girl waited till the next day before complaining to her sister of the attack made on her when she answered an office advertisement. It was not considered to be "the earliest possible moment," so there was no corroboration. No account was taken of the fact that the girl was shy and lived alone and was unable at once to see her sister, who lived on the other side of the city.

Since the war there have been more of the doubtful cases, such as one where it seemed more an excuse because she had not been paid and the man had gone off with her handbag.

Cases difficult to assess included those where the woman was slow or mentally backward and did not realize what the man was up to until it was too late to resist penetration properly.

Suspected Common Assault and Miscellaneous Cases

Some of these include borderline cases between rape and assault, but there were two cases of women over 70 years attacked in their rooms, one being in bed at the time. The cases in children were mainly those of cruelty by the parents or chastisement by adults. The numbers rose after the war to between 4 and 5 a year.

The miscellaneous cases were usually odd cases of abduction, of criminal abortion, of infanticide and abandoned babies, and of neglected and ill-treated children. One condition seen only since the war was sodomy, and in each case the man stated he had learnt the practice in the Army and had continued it with his wife or family after demobilization.

The Offenders

Apart from the men in the Forces, already referred to, the offenders range in age from young boys of 8 or 9 years to men of 70. With many of the lads it often seemed to be more inquisitive and experimental behaviour rather than real badness, but of course it does mean lack of training and teaching of decent behaviour at home. Then there are the old men and wrecks of men who are apt to hang round the parks, conveniences, and cinemas, and whose poor mental faculties are apt to be associated with somewhat perverted sexual feelings.

In the middle age groups there are a large number with I.Q.s probably between 70 and 80 who lack interests and occupations (which they got in wartime) and give way to various sexual urges, normal and abnormal. The majority of the cases of indecent assault are done by the hand only, though some are with the penis between the legs, and they chiefly involve sexually immature little girls of under 12 years (mostly only 5 or 6 years), so there is no advance or sexual response by the child. This indicates that some form of mental abnormality, defect, or perversion must be present—and these conditions are unlikely to respond to prison treatment.

Another type was the emotionally and sexually uncontrolled man who would rape the office girl or someone he had met at a dance or in the public-house as they went home. In many cases the effects of alcohol undoubtedly entered into the picture.

However much one feels that the men should be severely punished, the fact remains that prison will not cure a sexual perversion, though sometimes it may be necessary as a form of shock treatment to begin with. In a certain number, some form of psychiatric treatment may be possible, but the kind of condition likely to respond is limited. Moreover, the man must not only be willing but also mentally capable of co-operating with the doctor.

This makes it all the more necessary for the court to receive a medical and psychiatric report on the accused before sentence is passed, as was strongly advocated by the joint committee of the B.M.A. and Magistrates' Association in 1949 in their report on the criminal law and sexual offenders. Among other recommendations they suggested that, after guilt had been decided but before the sentence was passed, the courts "should be under an obligation, wherever possible, to seek the advice of a duly qualified medical practitioner with experience of this type of case, as it is only when furnished with an adequate report that it is possible to pass a suitable sentence. Possibly a team such as is found in a child-guidance clinic would give the best results." They also felt that more practitioners with the necessary qualifications and experience should be available.

Some cases could be dealt with by probation, with or without a condition of special treatment; but, again, to get good results it would need more psychiatrists and more probation officers to give adequate supervision.

There still remain the mentally and physically poor types who really need to be "cared for" rather than punished, as prison will not prevent further trouble arising. For these, as for some other types of mental defectives, I feel that the best place would be small homes within a colony where they could work and live according to their ability, protected and under supervision, and yet the public would be protected from their bad habits. Though expensive to set up and difficult to staff, in the long run it would probably prevent much damage and crime in the general community and eventually help to cut down the prison population and reduce the number of recidivists.

Points Arising

1. Women Police and Woman Police Surgeon.—It is clear that a large proportion of the examinations are of sexually immature girls under 12 years, of whom more than half are under 7. To take statements from these children that are accurate and full needs special qualities, and it is here that women police have shown their worth. A policewoman was always in the room with me, often before the statement was taken, as it is very important to get the examination done as soon as possible or slight corroborative signs may have gone for ever. Both of us being women, I am sure the child gave a better story, and one nearer the truth, than would have been given if either of us had been a man. Experience gained over the years by the surgeon can prove very useful in doubtful cases, and I feel very strongly that a woman doctor should be called in all cases of sexual assault. Women doctors, available now in almost all districts, could be given part-time appointments, as I was. And yet after 30 years I believe Manchester still remains the only place outside London where such an appointment

has been made, though there are a few places like the Manchester Division of Lancashire County where a woman is called in "in suitable cases." But as experience is very helpful and it is not everyone who wants to be bothered with possible court cases, a definite appointment probably gives best results.

2.—Court Procedure.—The aim should be to make conditions at court at least as good for the child witness as it is for the child delinquent, especially as in these cases she is often the most important witness. Everything should be done to reduce any further emotional damage. The following practices are helpful, and should be carried out in more courts than is done at present.

(*a*) In the cases of an adult offender where the juvenile court cannot be used, there is usually available a small room where there can be less formality, no dock, with everyone on the same level, and no great distance between the magistrates and the witness-box. Otherwise the atmosphere of a large court, the fencing round the dock, the high witness-box and magistrates' bench, and the numbers of strange folk present can be overwhelming for the child or young girl, who, in any case needs courage to give the unpleasant details of what has happened. It makes her more likely to get nervous and easily confused, and therefore more liable to appear to be an unreliable witness.

(*b*) A woman magistrate and policewoman should be required to be present in court in all cases of sexual assault.

(*c*) It should not only be possible, but compulsory, to clear the court in these cases, and publication of the names of the child witnesses should be prohibited, as with child delinquents.

(*d*) The cases should be brought to court as soon as possible. Delay in hearing or reference to sessions or assizes, with a wait of maybe weeks or even months, means that the child forgets the details of time and sequence and therefore gives a wrong impression, especially with a hard cross-examination. This holds good, too, where the witness is mentally slow or defective. The evidence while fresh in the mind can make such witnesses quite reliable, but the impression soon becomes hazy and then very patchy. Unfortunately the defence are not beyond taking advantage of this, as delay gives the accused a better chance of getting off. But it is bad for the injured persons, as a second appearance in court and repetition of their evidence tends to increase the psychological trauma from which they were possibly beginning to recover.

(*e*) An alteration in the law might be made so that a child who could not be sworn might be allowed "to affirm" the truth in suitable cases.

(*f*) Another alteration should make it possible to accept the unsworn evidence of a child if corroborated by one or more other children who have not been sworn.

3. Disposal of Accused.—As many of the accused are mentally slow or suffering from sexual perversion of some kind, it is clear that no amount of prison sentence is likely to stop them doing the same thing again on discharge. It is *treatment* of some sort with a view to *prevention* that is needed, rather than punishment, and this approach needs to be more fully realized by both the public and the courts. This means that it should be compulsory in sexual cases for the magistrates to get, before sentence, a medical and psychological report on the accused, in order that they can decide what is likely to be the best way of dealing with him.

Summary

This survey of cases seen over a period of about 27 years shows a large amount of sexual misbehaviour, particularly affecting girls of under 7 years.

Its management is helped by the presence of women in the Police Force. The necessity for the appointment of a woman police surgeon is pointed out if further trauma to the children is to be avoided.

The legal position of the child under 7 years and also the older mentally backward person needs careful consideration, and legal practice altered in some way if justice is to be done by them.

However, without further legislation much could be done to improve the way in which these cases are handled, both in and out of court.

CARBON-MONOXIDE POISONING

USE OF CARBON-DIOXIDE–OXYGEN MIXTURE

Statement by the Medical Research Council

In February, 1955, a report under the title of "Gases Administered in Artificial Respiration with Particular Reference to the Use of Carbon Dioxide" was published (*Brit. med. J.*, 1955, **1**, 313) by the Medical Research Council's Committee for Research on Breathing Apparatus for Protection against Dangerous Fumes and Gases, to explain the reasons that had earlier led the Council, on the advice of the Committee, to recommend the abandonment of the practice of carrying cylinders of carbogen (oxygen containing carbon dioxide) in ambulances.

The report confined itself to consideration of the first-aid treatment of patients in respiratory failure. The possible adverse effects on such cases of even comparatively low percentages of carbon dioxide in the inspired air were stressed and the report concluded with the recommendation "... that in first-aid practice carbon dioxide should not be administered with oxygen in the resuscitation of subjects requiring and receiving artificial respiration."

While accepting that pure oxygen was preferable to oxygen and carbon dioxide in the treatment of many cases of respiratory failure, Dr. H. L. Marriott (*Brit. med. J.*, 1955, **1**, 664) challenged this recommendation in so far as it related to carbon-monoxide poisoning, on the grounds that the administration of an oxygen–carbon-dioxide mixture caused increased elimination of carbon monoxide and quicker recovery.

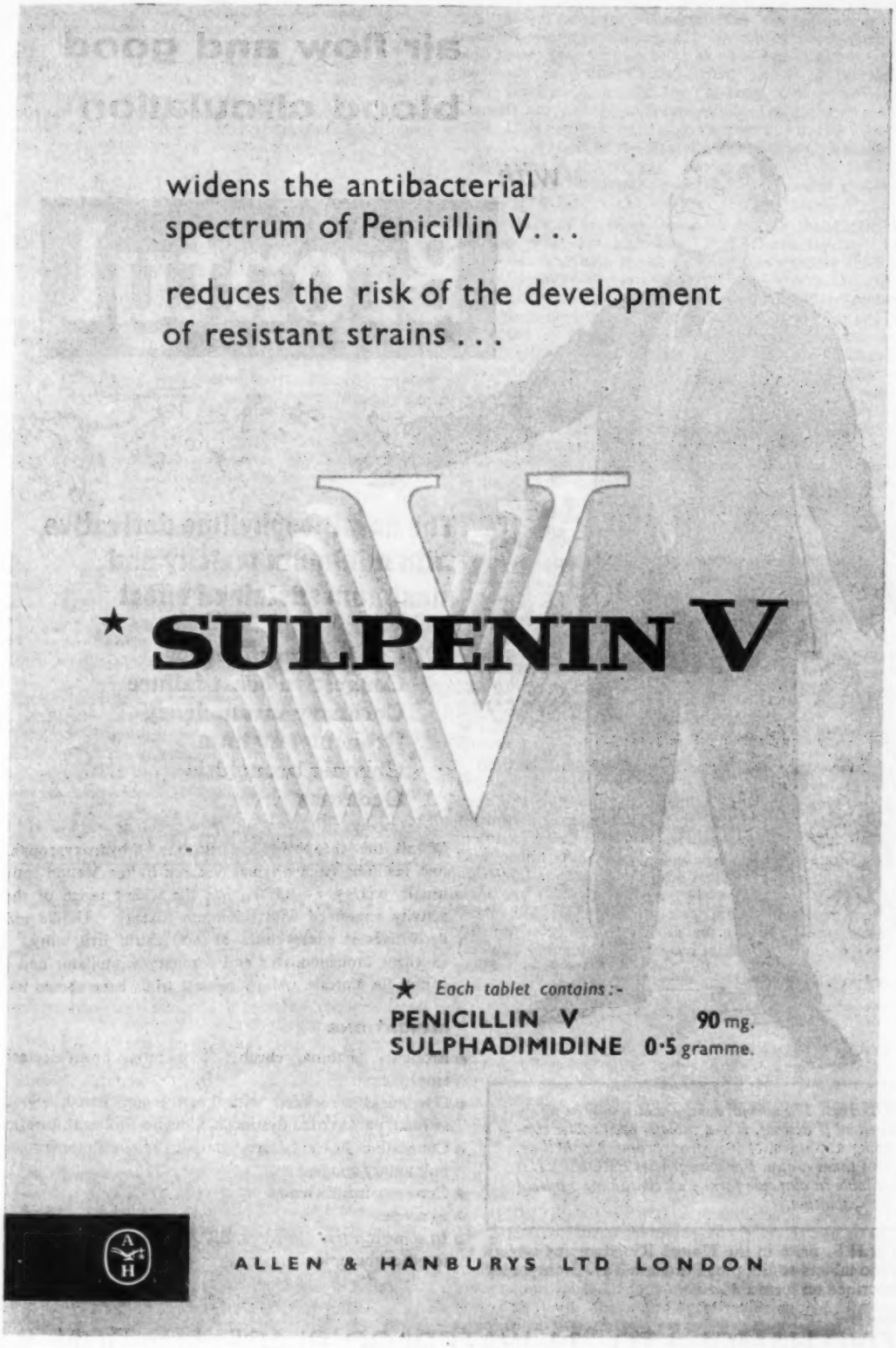
The Medical Research Council accordingly set up a special subcommittee of Council to "review all available evidence and to prepare for Council a statement for publication in the medical press." The following were appointed to this subcommittee: Professor Robert Platt (chairman), Sir Lindor Brown, Professor R. C. Garry, Professor J. McMichael, Sir George Pickering, Professor F. J. W. Roughton, Professor G. Payling Wright, and the Secretary of the Council, Sir Harold Himsworth.

Statistical Evidence

In view of the fact that mixtures of oxygen and carbon dioxide had been withdrawn from local authority ambulances in favour of pure oxygen as a result of the advice that they had received from their Breathing Apparatus Committee, the Medical Research Council had already asked Professor A. Bradford Hill to analyse the available mortality statistics on carbon-monoxide poisoning. If one method of treatment had any considerable advantage over the other, whether in patients with respiratory failure or not, it would be expected that the difference would be revealed in the statistics. Professor Bradford Hill published his report in the *British Medical Journal* (1956, **2**, 1220). After drawing attention to the limitations of the available data, and emphasizing that they were clearly not precise enough to prove the relative advantages (or disadvantages) of the oxygen–carbon-dioxide mixture compared with pure oxygen, he concluded that there was no evidence of any association between the number of registered deaths from carbon-monoxide poisoning and any change of practice in the treatment of such cases.

Respiratory Failure in Carbon-monoxide Poisoning

Members of the Council's Breathing Apparatus Committee have recently completed experiments on a number of species of laboratory animals in order to try to induce a state of respiratory failure by the administration of carbon monoxide. Although it is theoretically possible for an animal with carbon-monoxide poisoning to pass through a stage before death when respiration has failed but the circulation is still maintained, the experiments indicate by actual observation that, both in pure carbon-monoxide poisoning and in carbon-monoxide poisoning complicated by the prior administration of respiratory depressants, this stage either does not exist or is so short that it provides no opportunity for special treatment. Similarly, inquiries which the Council's subcommittee have made of those experienced in treating patients suffering from carbon-monoxide poisoning indicate that respiratory failure without circulatory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failure, as a definite clinical stage following carbon-monoxide poisoning, is very rare, if indeed it ever occurs; in the subcommittee's view, it is certainly not common enough to serve as the basis for deciding the method of treatment for all cases.

On the other hand, the results of the recent animal experiments, and of independent work on human volunteers poisoned with carbon monoxide but not to the point of respiratory failure, fully endorse the older evidence that the administration of a mixture of carbon dioxide and oxygen leads to a more rapid elimination of carbon monoxide from the blood than does the administration of oxygen alone.

Conclusions

After carefully weighing all the available evidence, the Council's subcommittee have concluded that the differences in practice between the effectiveness of the two methods of treatment are almost certainly small, but that, on balance, the evidence favours the use of a mixture of 5% carbon dioxide in oxygen for the treatment of carbon-monoxide poisoning. In the light of present knowledge the subcommittee do not consider that there is anything to be gained by the use of higher percentages of carbon dioxide in oxygen. The Medical Research Council have accepted the advice of their subcommittee and wish to issue the following statement:

> Experiments have clearly shown that, with either spontaneous or artificial respiration, the administration of a mixture of 5% carbon dioxide in oxygen leads to the more rapid elimination of carbon monoxide from the blood than does the administration of oxygen alone. The use of 5% carbon dioxide in oxygen for the first-aid treatment of carbon-monoxide poisoning would therefore appear to be preferable to treatment by oxygen alone. Pure oxygen, however, would appear to be preferable, as recommended by the Breathing Apparatus Committee in their report, for the treatment of those suffering from asphyxia and anoxia due to other causes, in which the administration of carbon-dioxide mixtures is contra-indicated. The Council have been assured by those with wide responsibilities for the supervision of first-aid services that it should not in practice be difficult for first-aid workers to distinguish between these two groups of patients; the circumstances in which the case is discovered will usually suffice to reveal its nature.

Motoring News

WINTER MOTORING ABROAD

While the majority of British motorists prefer to take their holidays during the summer months, there are many parts of Europe which enjoy mild weather during our winter. January and February are perhaps the two coldest months in Britain and those in which it is most desirable to travel south and seek the sun. It is unfortunate that the winter is not the easiest time for medical men to leave their patients, but, nevertheless, it is the best time financially to travel abroad. Hotels, restaurants, and all other facilities are cheaper, resorts are less crowded, and sunshine, if you go far enough south, is obviously beneficial to health, especially if it is at a time when it is lacking in Britain.

Ski-ing, skating, and other traditional winter holiday sports are, of course, available quite near at hand, but for the motorist there is little enjoyment in visiting a country which is well and truly snow-bound. An alternative is to go south on one of the regular steamships plying between Britain, East Africa, the Far East, and South America and alight at the first port of call. Passenger liners on these routes stop at such places as Vigo, Lisbon, Gibraltar, Casablanca, Genoa, and other Mediterranean ports.

Services to Vigo and Lisbon are maintained by Royal Mail, Blue Star, and Fanu Lines en route for South America. Each of these companies has one or two sailings a month from either London or Southampton. Passenger fares vary from £12 third class to £38 first for single rates, while there are special rates for children. The cost of taking a car amounts to approximately £23, on top of which dock dues and local taxes have to be paid. Sailings to Gibraltar may be made on Union Castle, Orient, and P. & O. ships *en route* for East Africa and the Far East. One or two sailings a month are made by each company and single fares are from £14. Cars can be carried at rates from £14 to £20 depending on size. Vessels of the Batavier line call at Casablanca and other ports in the vicinity. Passengers must, however, join the ship at Rotterdam, though cars are loaded at London. Passenger fares are £33 and cars £30, one way.

For sailings to Marseilles and Naples the Orient Line provide what are known as "amphibian tickets" which allow sea and land travel for passengers taking their cars. Single journeys to Marseilles and Naples with car and one passenger first-class amount to £81 and £89 respectively; four passengers on the same trip would be charged £160 and £189 for the same two ports, but in this case the car is transported free. A full car load is therefore desirable on this route, where, for under £50 a head, passengers enjoy a luxury Mediteranean cruise, travelling first-class, with the cost of transporting the car included. Naples, after all, is a long drive for motorists even after leaving the Channel ports. Incidentally, the cost of taking the car to or from France by the Lydd–Le Touquet air ferry is also included in these fares so that the holiday can begin or end with a sea cruise. Sailings are scheduled monthly to and from London.

To Genoa by the Union Castle Line first-class passenger accommodation costs £43 per person and a good tourist-class cabin £28. Cars are accepted at an approximate figure of £25 for a medium-sized model, but considerable reductions are to be made next year for passengers travelling first-class and taking a car with them. For motorists going to Spain, car freight is not so cheap. To Valencia and Barcelona a one-way passage for a car would amount to between £35 and £40, with passenger fares from £28. Sailings are made fortnightly from London and Liverpool by MacAndrews and Co. Ltd., and the ships also call at Bilbao, Lisbon, and Gibraltar.

Further information about these and other sailings is, of course, available from the national tourist offices of the countries concerned, and, while voyages of this sort seem expensive on paper at first, it is surprising what costs the motorist incurs when travelling hundreds of miles on Continental roads. A sea journey can obviate a lot of these incidental expenses, give each member of the party a five to eight day luxury cruise, and allow them to start motoring, fresh and relaxed, at some interesting southern port. Alternatively such trips can form an excellent substitute for the sometimes depressing homeward journey at the conclusion of the holiday.

IAIN GELLATLY.

Dr. William A. Horne, medical officer of health of the City of Glasgow, writes in his Annual Report for 1957 of the city-wide *x*-ray campaign, carried out between March 11 and April 12. During the five weeks of the campaign some 715,000 persons were *x*-rayed, of whom 622,349 were Glasgow residents. Among the Glasgow residents 2,369 active cases of pulmonary tuberculosis were found, giving a rate of 3.7 per 1,000 over 14 years of age. The total number of new cases of pulmonary tuberculosis notified during the year was 3,925 compared with 2,024 in 1956. The highest incidences were in young adult women and in men in the older age groups. During the five weeks of the campaign 30,506 persons were recalled for further examination on large films—a recall rate of 4.3 per 1,000. Some 58% of these presented evidence of significant radiological abnormality requiring further investigation or medical supervision. 347 sufferers from lung cancer were found, the highest incidence being in men over 60.

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Influenza Virus A (Asian) Vaccine (Parke, Davis and Co., Ltd.).—This is a vaccine made by growing the 1957 (Asian) strain of influenza A in fertile eggs, inactivating with formaldehyde, and making up in aluminium phosphate suspension. It is prepared at the Wright–Fleming Institute, St. Mary's Hospital.

Invirin (Glaxo Laboratories Ltd.).—This is a similar preparation containing in addition to the Asian strain a 1956 A strain and a B strain. Since it is likely that most of any serious influenza occurring in the general population in the near future will be caused by a strain related to the Asian, the usefulness of the other two viruses is doubtful.

Such vaccines are best given in 1-ml. doses, deeply subcutaneously; children require smaller doses. They should not be given to persons sensitive to egg protein. The vaccines are stable only if kept in the cold (2–10° C.—35–50° F.). They are best given in December, since, in contrast to 1957, most influenza outbreaks occur in January and February. Recent trials in several countries indicated that vaccination led to a reduction in incidence of influenza to one-third of that in controls: better results than that cannot be expected at present. Immunity is not likely to last for more than one winter. As indicated lately (*Journal*, September 20, p. 732), there are grounds for hoping that we may escape a major outbreak of influenza this winter.

N.H.S. basic price: Influenza virus A (Asian) vaccine, 1 ml., 4s. 1½d.; invirin, 1 ml., 7s. 6d.

Ilotycin Glucoheptonate I.V. (Eli Lilly & Co.).—This is a preparation of erythromycin for intravenous injection. The contents of a 250-mg. ampoule are dissolved in 10 ml. "water for injection" (not saline). This solution can be injected slowly without further dilution or added to saline or dextrose solution for continuous infusion. A dose of 250 mg. or more up to 1 g., according to the severity of the infection, is administered every six hours. Dilute solutions can be instilled into body cavities. The preparation is not suitable for intramuscular or intrathecal administration.

This form of the drug is indicated when oral administration is impracticable for the time being; it has the added advantage of producing high concentrations in blood and tissues certainly and rapidly. Erythromycin has a similar range of activity against ordinary bacteria to that of penicillin, and may be indicated for the same infections (e.g., lobar pneumonia, any haemolytic streptococcal infection) when the use of penicillin is contraindicated as, for instance, in sensitized patients, or when the causative organism is resistant to penicillin, as is now frequently the case in staphylococcal infections.

N.H.S. basic price: 250 mg., 15s.

"It was interesting to read that a doctor who is police surgeon at South Shields, and has one of the largest practices there, has been given the sub-postmastership of an area of the town. . . . Any solicitor who wishes to engage in other professions or businesses will find guidance as to what he may and may not do in a lecture on professional conduct and etiquette, delivered by the secretary of the Law Society. The broad principle is that he may carry on any honourable profession or business, for example as a stockbroker, or coal merchant, or manager of a theatre. But apparently not as a publican, or licensed moneylender or pawnbroker, or bookmaker."—*Law Notes*, November, 1958, p. 263.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Medical Charities

SIR,—The registration of the Charities Trust Fund of the Association as a charity, resolved by the Council during last session and announced at the A.R.M. at Birmingham, is complete. The most important consequence is that the Trust is enabled to receive covenanted subscriptions which when a promise of seven consecutive years' payment is made allow income tax to be recovered at standard rate. Herein lies a great opportunity to increase the receipts of the charities of the profession without extra cost to the donor.

We are deeply appreciative of the generous support of members of the profession, and we understand that many already subscribe, under covenant, to the various charities of the profession. We suggest, however, that those who do not already subscribe under covenant should consider carefully whether they could not do so, whatever the amount. Most contributions are made when the annual subscription to the Association is paid, and on the application form this year will be found a "box" for indicating that the donor will undertake a covenant. If this is filled in, the necessary forms will be sent for completion of the formal promise.

Applications for help from the aged and sick members of the profession and from widows and orphans are greater than ever, and the need in each case is increasing. We appeal to all members to support the worthy cause of medical benevolence, especially by covenant through the Charities Trust Fund. The B.M.A. Charities Committee is a collecting body which advises the Council on the best method of distributing to other charities the moneys it collects in the Charities Trust Fund.—We are, etc.,

S. WAND,
Chairman of Council.
L. DOUGAL CALLANDER,
Treasurer.
H. M. GOLDING,
Chairman of Charities Committee.

B.M.A. House,
Tavistock Square,
London, W.C.1.

Trypanosoma rhodesiense in Bushbuck

SIR,—I have just read with great interest the paper by Dr. R. B. Heisch, Mr. J. P. MacMahon, and Dr. P. E. C. Manson-Bahr and your annotation thereon (*Journal*, November 15, pp. 1203 and 1211). As one long interested in this subject, will you allow me to submit some comments that may help in reviewing the available evidence on the nature and origin of the trypanosomes of man? On the inoculation of game trypanosomes into man you write: "This essential test was not applied by the early workers." The following facts are, I think, relevant. In 1919 Taute and Huber, in German East Africa, inoculated 129 Africans with *T. brucei*: none of these men became infected.[1] In 1930, in Tanganyika, Corson was accidentally infected with *T. rhodesiense*; a year or so later he infected himself with *T. rhodesiense*. On each occasion treatment was fully effective.[2] In 1932, in Uganda, I exposed three Africans and one European to cyclically infective *G. palpalis* carrying a polymorphic trypanosome obtained from a situtunga antelope on the Sesse Islands on Lake Victoria. None of the men became infected.[3] In 1933 Fairburn in Tanganyika infected himself with *T. rhodesiense*; and again drugs effected a prompt cure.[4] Both Corson and Fairburn also employed African volunteers.

Turning now to the paper, which records the first recovery from wild African game of a trypanosome pathogenic to man. That "only one serious attempt to isolate polymorphic trypanosomes from game animals has hitherto been made" is, however, an understatement. The Royal

Society's Commission early in the century, and later on the Trypanosomiasis Research Institute and the League of Nations Commission, were all engaged in this line of research in Uganda. In the present authors' successful experiment a polymorphic strain was recovered from each of two bushbuck. One of these strains proved infective to man and the other was not. The successful inoculum into man consisted of 25 ml. of rat's blood, heavily infected with parasites (over 100 per oil-immersion field). Note the mode of infection—direct blood inoculation as distinct from fly transmission. My experience of cyclical transmission strongly suggests that development in the fly may influence the host-propensities of a strain. Moreover, cyclical transmission is the natural mode of infection, and it is extremely doubtful whether anything like the concentration of parasites present in the 25 ml. used in the experiment would be introduced by a feeding tsetse. In other words, flies infected with this strain *might* fail to infect man and the trypanosome would then be regarded as *T. brucei*.

An experiment carried out in Uganda is of interest here. Two antelopes were infected, each with a different strain of *T. rhodesiense*, and each animal was then exposed to clean tsetse, each fly-cage being fed on the one antelope only. These flies subsequently proved invariably infective to laboratory animals and non-infective to human volunteers. When, however, the blood of the antelope, taken at the same time as the fly-feeds, was inoculated into monkeys, clean tsetse infected from these monkeys infected the majority, *but not all*, of the volunteers on whom they were fed.[5] Another experiment illustrated still further the variability of the factors involved. A strain of trypanosome taken from a man's blood was introduced into an antelope, monkeys, and small laboratory animals and studied for some years at the Trypanosomiasis Research Institute. During that time nine different volunteers were exposed to infection with this strain by the cyclical route, many of the flies having acquired their infection from monkeys; none of these men became infected. A bushbuck was also infected with this strain, and some 2½ years later this animal's blood was injected into and infected a monkey. Blood from this monkey was injected into two volunteers and both became infected.[6] Yet another variable factor is the susceptibility to infection of different species of antelope. Corson[7] found one species of reedbuck more susceptible than another, and in Uganda we found bushbuck and reedbuck more liable to infection than situtunga and oribi.[8]

All these observations suggest that the balance between susceptibility and resistance to trypanosomes is in man very finely adjusted and sensitive to minute physiological changes in host and parasite and possibly tsetse. In view of all these variables I submit that it is not yet possible to decide whether *T. gambiense*, *T. rhodesiense*, and *T. brucei* are one or different species. My own view still is that *T. brucei* is a potential parasite of man; that its normal hosts are game animals; but that, given adequate opportunity, it can adapt itself to man. Its supreme achievement in this direction is the form known as *T. gambiense*.—I am, etc.,

Cross-in-Hand, Sussex. H. L. DUKE.

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Pharmaceutical Houses and the Doctor

SIR,—I read Dr. Mary M. Rayner's letter (*Journal*, November 22, p. 1291) with a mixture of astonishment coupled with a sense of despair, and finally cynicism. I really wonder if, in addition to completing questionaries and writing letters to the *Journal*, your correspondent reads it. If she does, I fail to understand how, in her letter outlining her difficulties, she can fail to refer to the *British National Formulary*, now in its fourth edition, the alternative edition of which was favourably commented upon in your columns only a few weeks ago (*Journal*, September 6, p. 601).

The Joint Formulary Committee of the B.M.A. and the Pharmaceutical Society, established in 1946 and on which I have served for more years than I care to remember, has the task of compiling, reviewing, and making appropriate additions and deletions of drugs and preparations of value for use in hospitals and proved in medical practice throughout the kingdom. Of course the doctor is still left free to prescribe outside the *Formulary* if he considers it to be in the best interests of his patient.

The *British National Formulary* is a cheap, small, pocket-size book, and in it Dr. Rayner will find 9/10ths of what she so plaintively requests. The 4th edition, 1957, and the amendment, 1958, puts into the hands of practitioners a proved useful list of preparations adequate for all purposes. There is no need for Dr. Rayner to attempt to compare the "more expensive proprietary antibiotics": she can, I submit, select from the *British National Formulary* all that is required for her sick patients, and this without reference to the charming young representatives of the pharmaceutical houses whom—in her innate courtesy—she finds so difficult to resist. Nor need she refer to the postal advertising efforts, with or without samples, all of which could be consigned to the waste-paper basket and her patients none the worse. If she feels that she may be a little behind the times in her prescribing, she can be assured that any proved and worthwhile preparation will quickly find its place in the *British National Formulary*. In the alternative edition she will find the same material classified upon a pharmaceutical basis, and brief introductory monographs usefully discuss the pros and cons of the particular choice of drug within the group to be used. In both editions lists of proprietary drugs with their equivalent official names and *per contra* lists of official names with the corresponding proprietary names will be found.

Dr. Rayner should also find the *Prescribers' Notes*, issued regularly by the Ministry of Health since 1952 and sent to all doctors on the executive council lists, of considerable help. If this is not enough, reference may be made to the Ministry of Health publication *Proprietary Medicines*, compiled by the Standing Joint Committee on the classification of proprietary preparations and prescribing (Cohen Committee). Surely this is exactly the "body of men to deal with all these proprietary products" for which Dr. Rayner pines. They too have been working for many years. Their latest list was published in 1957. Of the six categories of preparations listed, Dr. Rayner should be particularly interested in: Category 1—"New drugs of proved value not yet standard," and Category 5—"Preparations not in the *B.P.*, *B.P. Codex*, or *B.N.F.*" which in the Committee's view have not been proved of therapeutic value. The *British Pharmacopoeia*, the neglect of which Dr. Rayner deplores, is essentially a book of standards, invaluable for occasional reference, but not likely to appeal to the busy general practitioner.

Finally, I can assure Dr. Rayner that a large number of final-year students now walk round the wards with the *B.N.F.* alternative edition in their pockets, are encouraged to write prescriptions from it and to use official names. Moreover, the Ministry of Health, concerned about prescribing costs, and following part of the advice given by the Hinchliffe Committee on prescribing, is about to provide every final-year student with the *B.N.F.* (alternative edition, I hope). He will then be "the proud possessor of a good (if compact) pharmacopoeia" as Dr. Rayner hopes, and able to "hold his uncovered head high in general practice," and if he so chooses to resist the blandishments of both the representatives and the advertising methods of the pharmaceutical houses if he finds them objectionable.—I am, etc.,

Department of Clinical Medicine, University of Leeds. S. J. HARTFALL.

*** Professor Hartfall might have added "To-day's Drugs" and the series on "Drug Treatment of Disease," appearing each week in the *British Medical Journal*, to his list of up-to-date sources of information on drugs.—ED., *B.M.J.*

SIR,—Dr. Mary M. Rayner (*Journal*, November 22, p. 1291) describes herself as a simple family doctor, and certainly her polemic against the pharmaceutical industry is unreal and inaccurate. She and some other critics of that industry have a blind spot for two basic facts. First, we live in a relatively free economy; and for as long as we do, for so long will the structure and mode of operation of the industry conform by and large to their present pattern. If Dr. Rayner wants a controlled economy, let her say so; but

it would be invidious and impracticable to single out the production and selling of drugs for a treatment not also to be given to, say, the motor-car or farming industries or—dare I say it?—to the medical profession. Second, this *Journal* and others often contain justified grouses from doctors that they are not paid enough by the N.H.S. A Royal Commission is sitting on the topic at the moment, and evidence is being most skilfully given to it by doctors: that is, the profession wants more money, and is using all legitimate means to ensure that it will get it. Why is it wrong for a pharmaceutical manufacturer to do the same? Dr. Rayner really cannot have it both ways. Simple business men often say to me, "You doctors do a better public relations job for yourselves than any other group in the country"; and, of course, the present Minister in charge of Government propaganda is an ex-secretary of the Association.

Dr. Rayner suggests there should be some central body to assess the value of drugs for the simple general practitioner. Well, there is "To-day's Drugs"—in my view an earnest and well-meant feature. There is the *National Formulary*; there are *Prescribers' Notes*; there are the opinions of consultants, praised by Dr. Rayner but often in my experience based on a careful study of the glossy pharmaceutical literature decried by her. (What, by the way, is wrong with its being glossy? Should it be the kind of economy paper we had during the war in a controlled economy?) Excessive centralization in the matter of assessing new drugs might have drawbacks worse than its possible advantages. Most people, and many doctors, hate innovation; so do official and authorized bodies. That is why most major advances in any field come from a single man with a single "crackpot" idea: a new and embryo penicillin would hardly survive scrutiny by a Government committee ("Think of the cost . . .," "Importance of the body's natural defence mechanisms . . .," "Current Ministerial thinking . . .," "Over-population . . ."). I experienced official therapeutics when in the Army. While appreciating the need for it in wartime, I disliked it, and so did every other doctor I met.

Let pharmaceutical firms, says Dr. Rayner, "start measuring their products against each other's scientifically." They already try to do so. Clinical trials are an essential element in scientific assessment of a drug; but every pharmaceutical manufacturer daily laments the difficulty of obtaining those clinical trials that will provide the very evidence on a drug that doctors demand from him. I am *inter alia* medical adviser to a pharmaceutical firm, and have it as a rule of thumb that, if one desires a single paper on a new and interesting drug, one must initiate at least six separate clinical trials. Five, started in good faith by both manufacturer and clinician, and at some cost to the former, fall by the wayside. Why? Not because of any lack of enthusiasm in the firm making the drug. This may be an unpalatable fact, but it is a fact.

Dr. Rayner deprecates salesmen and advertisement psychologists (whatever they may be) and free gifts. The use of all these is merely a way of bringing the attention of doctors to a new and useful drug, and of securing their good will. Only if a substantial demand develops does manufacture of a drug become economically worthwhile—with the possibility of price reduction. The best drug in the world will never be used widely unless it is advertised in the fullest sense: we hate innovation. Aspirin was discovered 30 years before any doctor began to prescribe it; and paracetamol for 40. D.D.T. lingered, unsung, for as long; the discovery of penicillin went unexploited for 12 years. "Exploitation," what a dreadful word?—but it meant lives saved by penicillin as well as profits for its manufacturers. Dr. Rayner may not like the implications of these facts; but she ought to face them. And may I suggest that advertisement, perhaps of a more discreet and subtle kind than any practised by the industry, is not unknown in the profession? Have we not a thing called a bedside manner? Do doctors, having published a good paper in a good journal, disown it? Or do they very properly see that the right quarters are at the right time appraised of the paper's existence? Dr. Rayner criticized the shiny new cars of pharmaceutical representatives. Should she really prefer dirty old cars? Of course the cars cost money, and of course the good manufacturer makes the money by selling drugs; but that is what life, in the material sense, is about in this country in 1958.

I should like to end with a few more facts. The *British Pharmacopoeia* (and Dr. Rayner thinks it good for a doctor to have one, and I agree) is now largely written with the gladly given assistance of the pharmaceutical manufacturers. They have discovered the new drugs that are to be canonized by inclusion in the *B.P.*, and they know more about those drugs than anyone else. The "rising drug bill": between 1949 and 1957 it increased from 35 to 73 million pounds; in the same period hospital costs went up from 219 to 421 millions. I leave Dr. Rayner to draw a simple conclusion. The pharmaceutical industry in this country says it can afford to spend only 4 million pounds a year on research: the figure in Switzerland [*sic*] is 7 millions. The British industry sells 45 million pounds' worth of drugs to the N.H.S. at manufacturers' prices: it exports 40 million pounds' worth. (Does Dr. Rayner favour exports? And does she think foreign countries are influenced to order drugs from the British industry when it is stigmatized by a British doctor as trying "to degrade our profession," and as practising "wiles and subtleties"?) Between 1953 and 1957 the index of prices for branded drugs fell from 100 to 82: the index of general retail prices rose in the same period from 100 to 116. A voluntary price regulation scheme for branded drugs has already been formulated by the industry and the Government. It affects 90% of the cost of all N.H.S. proprietary drugs. The estimated saving?—about £350,000 a year. Will Dr. Rayner agree that the smallness of the saving may mean that the previous prices were not in fact excessive? Or does she accuse the Treasury of a lack of financial acumen?

Dr. Rayner and Dr. Charles S. Thomson (*Journal*, November 22, p. 1291) imply that pharmaceutical manufacturers are lacking in responsibility, unlike doctors. Who do they imagine these dreadful manufacturers are? They are in fact ordinary men and women, getting considerable satisfaction from the making and selling of drugs that will save lives and shorten disability; and they have as much sense of responsibility as any other citizen. The pharmaceutical industry, for instance, is well known to give more, relative to its size, to charitable and academic good causes than any other industry in this country. Far from inciting her colleagues to "unite and fight these pharmaceutical firms," Dr. Rayner should try to realize that without them present-day medicine simply could not exist. The industry and the profession are partners in a great enterprise, not enemies. Of course the industry has some defects, as we all have. It knows it has them. But they will not be remedied by ill-informed criticisms or by suggestions of sweeping Utopian alternatives, dreamt up perhaps "on a Monday morning, during a crowded surgery."—I am, etc.,

S. BRADSHAW,
Medical Adviser,
Aspro-Nicholas Ltd.,
Ethical Pharmaceuticals Division.

Normandy,
Near Guildford.

SIR,—I would like to thank Dr. Mary M. Rayner (*Journal*, November 22, p. 1291) for a very excellent letter regarding the effect of high pressure advertising on the G.P. She is a shrewd observer and has placed a very adept finger on the main cause of the cost of the drug bill. The possession of Martindale's *Extra Pharmacopoeia* is, in my opinion, an absolute must in general practice, and if the Ministry were to supply each G.P. with one gratis it would at the very least earn its keep and at the best would save pounds per head per annum.

However, I would not like it to be felt that this means that all the drug houses are selling useless products at high prices. This of course, as all know full well, is far from the truth; indeed, a casual perusal of "Martindale" will show, if prices in the *Drug Tariff* are compared, that many of the proprietary preparations are cheaper and better, and in many cases that no equivalent is available. However, many readers will be as staggered as I have been recently to find that many of the so-called "new" pain-killers are no more than our old pals aspirin and phenacetin when the mumbo jumbo of their chemical formulae is reduced to an intelligent level. There has been in some instances a definite attempt to blind us with science in the form of chemical *noms de plume*. Reference to "Martindale" will show

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at once to which particular section or type a particular substance belongs.

Pharmacology and Materia Medica have now grown so vast and vital that a serious attempt should be made to offer to G.P.s either refresher courses—with adequate locum coverage—or a monthly "digest" compiled and edited in an attractive way to combat "Big Brother" techniques.—I am, etc.,

Shipley, Yorkshire. J. A. FRAIS.

SIR,—As a representative for the last 44 years with a firm of surgical instrument and equipment manufacturers, I feel that drug house representatives who visit the general practitioners have been handed out rather a raw deal in your correspondence columns during the last year, and now one of your latest correspondents, a lady doctor (Dr. Mary M. Rayner, *Journal*, November 22, p. 1291) considers them ideal companions at a dance or cocktail party, but can give them only two minutes, out of courtesy, for a discussion on new medical preparations.

My experience suggests that most of the representatives are qualified chemists and members of the Pharmaceutical Society, and rank with hospital pharmacists, from whom the doctors are glad to obtain information on new drugs, dosages, etc., when working in hospitals.—I am, etc.,

Stockport, Cheshire. R. MERRYWEATHER SHAW, Pharmaceutical Chemist.

Pharmaceutical Houses and the Postman

SIR,—During October I kept all the advertising matter which arrived at the surgery used by our partnership of three. Not counting the duplicates which arrived at our home addresses, I collected 235 packets which weighed in all exactly 14 lb. (6.4 kg.), and on which the total postage was £2 2s.

What an opportunity for the statistician! If we are 1/7,000th part of the N.H.S. practitioners, it works out during the course of one year that 21,000 doctors receive 19,740,000 packets weighing 525 tons (1 ton = 1,016 kg.), and on which the postage is £176,400. Or, to make it even more fantastic, let us take 63,000 registered medical practitioners receiving 59,220,000 packets weighing 1,575 tons and the postage is then £529,000. Imagine the numbers of postmen carrying this mountain of paper! Imagine the numbers of refuse collectors carrying it all back again (probably mostly unopened)! Imagine the chemists getting in supplies of the new wonder drugs, only using them once, and then keeping them on their shelves.

I wonder how much of this enormous expense goes on the national drug bill, or alternatively reduces the drug firms' taxation? And do our patients get any better treatment because of it?—I am, etc.,

Tynemouth. J. PHILLIPS.

SIR,—May I plead that all those many firms who send us advertisements should respect the very difficult task of the postal authorities during the fortnight before Christmas, and refrain from advertising their products during this period.—I am, etc.,

London, S.W.1. FRANCIS LESLIE.

Rational Use of Drugs

SIR,—I have followed with great interest recent comment on drug pricings and overprescribing. Contrary to a recent observation on the teaching of medical students in the use of *National Formulary* preparations, I was taught to use the *N.F.* whenever possible. However, on my first "sedative round" I found tab. butobarbiton. was not available. The next day the hospital pharmacist told me that "soneryl" tablets were bought by the hospital group on a bulk contract, and were thus cheaper than tab. butobarbiton., *N.F.* Similarly, in another hospital my attempt to order caps. vitaminor. was frustrated. "Multivite" was the available preparation, again on bulk contract.

It is difficult to find up to date and authoritative information on the new preparations as they become available. The *Practitioner* publishes an excellent series on new drugs, and this I find most helpful. Your new series "Drug Treatment of Disease" similarly has been very helpful, but like Dr. D. R. Laurence (*Journal*, October 11, p. 914) I was disappointed in "To-day's Drugs."

Occasionally having access to the *Journal of the American Medical Association*, I find the pronouncements of the Council on Pharmacy and Chemistry are authoritative and without bias, either commercial or political. Surely we could well do with a similar organization here? I would like to press for the formation of a Council on Pharmacy and Chemistry, under the auspices of the B.M.A., modelled on the lines of the American one, submitting regular reports on drug action and uses to the *British Medical Journal*. How else may we sort our present problems, which increase each day with the morning post?—I am, etc.,

Blandford, Dorset. GEOFFREY F. BAINES.

Petrol-vapour Poisoning

SIR,—It would seem from the comments made by Dr. Reed Aidin in his article (*Journal*, August 9, p. 369), and Dr. B. George in his letter (*Journal*, October 18, p. 979) concerning the dearth of published accounts of petrol-vapour poisoning that this form of intoxication may be less well known in civil life than it is in the Royal Navy. During the second world war fairly frequent cases of petrol vapour poisoning were reported, but once the nature of this hazard was recognized and the methods of protecting against it were promulgated it usually ceased to be a hazard.

Typical incidents are cited in the *History of the Second World War*[1] in His Majesty's Ships *Victorious, Activity, Glenroy, Empress,* and *Arbiter,* in which there were several fatalities. Attention is drawn in the *History* to the insidious danger of a steadily rising concentration of petrol vapour which, in contrast to sudden exposure to an irritant high concentration of vapour which is quickly recognized, deadens the sense of smell so greatly that the danger is not detected by the unwary; and also to the fact that complete protection is only afforded by a self-contained breathing apparatus which does not rely on the ambient air for its support, such as the Salvus, although the conventional Service respirator for protection against chemical warfare agents, which every Service man has in his possession, affords good protection for the very useful period of 10 minutes. The need is emphasized for efficient ventilation arrangements in the construction of petrol control compartments, and for ensuring that ventilation systems are cleaned and maintained efficiently.

Dr. Aidin's comment that the accident he reports happened on a warm day is of particular interest, and underlines the need for increased caution when those exposed to petrol vapour are working in a warm atmosphere indoors or in a hot climate.—I am, etc.,

Medical Department of the Navy, London, S.W.1. F. P. ELLIS.

REFERENCE

[1] Ellis, F. P., *History of the Second World War, United Kingdom Medical Series. Medicine and Pathology*, edited by V. Z. Cope, 1952, p. 312. H.M.S.O., London.

Advising the Bronchitic

SIR,—Personal experience is of much greater value than second-hand information. Having suffered from chronic bronchitis almost all my life, I consider myself able to speak with authority on this important subject. It is indeed a very sad fact that only a small percentage of the medical profession realize that certain "chesty people" are hypersensitive to any forms of tobacco smoke (especially pipe tobacco).

During my daily work as a chest physician I often inquire from my smoking patients if they can travel on the top of

a bus or tram. The bronchitic and asthmatic invariably reply, "No. Because it makes me cough." Yet these same people admit to smoking 10 to 15 cigarettes per day. Is it any wonder they cough? They fail to see that they are producing the very same atmosphere they cannot tolerate on a bus. Patients are always ready to blame the weather or their employment but never their smoking habits. If these patients were advised to stop smoking, there would be less of them suffering from chronic bronchitis and persistent coughs. Cutting down is not enough, they must stop smoking altogether and avoid smoky atmospheres. I am also often asked, "Shall I stop smoking cigarettes and start pipe smoking?" I always reply that from the health point of view pipe smoking is worse because it produces four or five times the amount of irritating fumes.

But what of the other unfortunate victims who do not smoke and yet have to inhale these fumes? The greatest calamity which can befall them is to be admitted to a hospital ward or convalescent home in this country. Recently an emphysematous patient was admitted to a local convalescent home. She was compelled to sit half-way up the stairs during the daytime, this being the only place free from tobacco smoke. Another patient was compelled to forgo her hospital gastro-intestinal investigations—because of the smoke from the other female patients. It is high time the hospital management committees throughout the country woke up to these facts and provided side wards on every medical and surgical ward where patients who so desire may have their treatment in an atmosphere free from pollution with tobacco smoke.—I am, etc.,

Leeds, 8. DAVID A. HERD.

Qualified Pen-names

SIR,—I was intrigued when I first read about the B.M.A. booklet on nutrition by John Clyde, M.D., etc., and when my wife obtained a copy my curiosity got the better of me. I looked him up in the *Directory*. Imagine my surprise when I found no such name. There only were the three of us. One I have met, the other I have not had the pleasure of meeting. I wondered what mysterious motive the B.M.A. could have in sponsoring work done by some nebulous nobody, and I must admit that my confidence in the integrity of the B.M.A. received a little jolt on discovering their apparent duplicity (or quadruplicity). Should the booklet not have contained the usual writer's disclaimer that all characters mentioned in this book are purely fictitious and have no reference to any person living or dead?

As Sir Stewart Duke-Elder implies in his letter (*Journal*, November 29, p. 1355), I also feel that you cannot escape some responsibility for helping to make three into four and thereby reducing each by a third, because if I remember right I first saw reference to this new member of our clan in the columns of the *British Medical Journal*. Has the B.M.A. been doing some roamin' in the gloamin' by the bonny banks?—I am, etc.,

Bordon, Hants. N. P. R. CLYDE.

Poliomyelitis Vaccines

SIR,—Dr. Ritchie Russell (*Journal*, November 29, p. 1354) in discussing our review of the present position of live poliovirus vaccines (*Journal*, November 15, p. 1184) says that it is doubtful if we presented a balanced analysis of the present position. We did not, as he suggested, condemn live poliovirus vaccines, nor did we take a strong line against trials. We said that it was unlikely that any country with the finances available to undertake a vaccination programme using formalinized vaccines would use or switch to attenuated virus vaccines until it has been shown that they are as safe as, or safer than, formalinized vaccines and produce as good or better levels of immunity. We said that live virus vaccines appear suitable for trial in countries where formalinized vaccines cannot be afforded, and we said that in our opinion carefully conducted trials of attenuated virus vaccines should be undertaken in such countries if there is a genuine need for vaccination.

We tried to indicate that human vaccine viruses which (*a*) change their characteristics after growth in the human host and (*b*) spread readily to contacts are a new concept and therefore may not be easy to evaluate.

Dr. Ritchie Russell apparently thinks that we place more weight on the results of monkey pathogenicity tests as an indicator of potential neurotropism in man than in fact we do. Admittedly we are worried when the laboratory characteristics of excreted virus resemble those of some wild viruses the stability of which is at least questionable. What is important is that the virus excreted by some vaccines differs from the original virus and can spread to contacts. With this knowledge, we consider that the safety of the excreted virus should be subject to the same type of preliminary clinical trial as the original vaccine virus.

Dr. Ritchie Russell discusses the effect which different vaccines may have on the natural history of the poliovirus. We, too, are interested in this problem but like him can only speculate.

Dr. Ritchie Russell asks us to clarify our hopes and fears. Our hopes as far as vaccination against poliomyelitis is concerned are the same as his—namely, that, safe, efficient cheap vaccines will be available in all countries. We cannot see that a live vaccine must necessarily fill this bill, and we think that improvements will certainly be made to the inactive virus vaccines at present in use. Our fears are that, unless trials are carefully conducted to test the safety of living virus vaccines, the future of these vaccines and perhaps public confidence in all poliovaccines may be jeopardized.

Dr. Ritchie Russell must be irritated by the many delays and alarms that have accompanied the development and trials of oral vaccines. He would like to see the oral vaccines put to the test quickly and decisively. We share his sense of urgency, but obviously disagree on methods of assessing safety and effectiveness, neither of which we take for granted.—We are, etc.,

Department of Microbiology, The Queen's University, Belfast. G. W. A. DICK. D. S. DANE.

Onset Enuresis

SIR,—The excellent publication by Drs. J. D. Paulett and E. Tuckman (*Journal*, November 22, p. 1266) prompts me to mention a case of enuresis which I have always considered one of those we would like to meet more frequently.

It was 1942, and we had well over 200 unbilletable enuretic evacuees in various hostels in Cornwall. Onset enuresis was not a major problem, for out of that segregated number only one had failed to give a positive answer to my stock question: "And what did your mother say when you wetted your bed at home?" The last batch of children had been sorted out, and six months had passed without any further complaint from a billeter. I was therefore all the more annoyed when a 12-year-old boy was reported to have started wetting his bed.

I found a healthy and intelligent youngster waiting for me, who was obviously greatly upset over his misbehaviour. He admitted having wetted till the age of 5, but there had been no lapses after he had started school. He had an elder sister who had remained with his parents. Neither at his school nor at his billet could any cause for this sudden change be found, and he had appeared to all and sundry as happy as ever. Yet for the past six nights he had never once been dry. He was clearly eager to give me every assistance, but, after my inquiries had drawn a blank all round, his face began to assume a look of helpless resignation. It was then that I fired my last shot: "When did you get your last letter from home?" "A week ago to-day." "And what did it say?" "Mum said I had a baby sister."

He went back to his billet and was never wet again.

—I am, etc.,

London, W.1. W. E. R. MONS.

SIR,—In their interesting study (*Journal*, November 22, p. 1266) Drs. J. D. Paulett and E. Tuckman state that there is "no information in the literature on the prevalence of the onset type of enuresis." They are evidently unaware of the important studies of Dr. Bertil Hallgren, of Stockholm. In the first of these Hallgren[1] reported the results of a survey of 1,992 unselected primary school children. Of these, 205 had a history of nocturnal enuresis occurring after the age of 4 at least once a month, mostly several times a week, and of these children 86 (42%) had earlier been dry. The frequency of onset enuresis in this sample of schoolchildren

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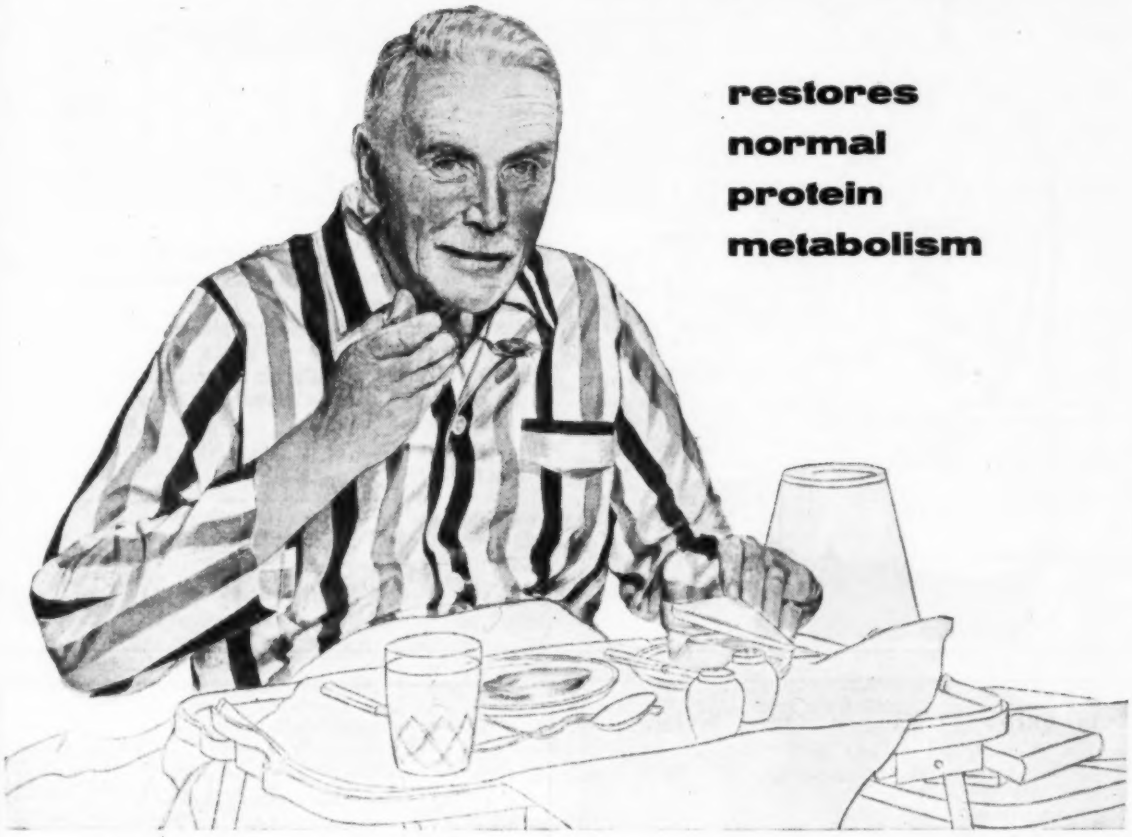

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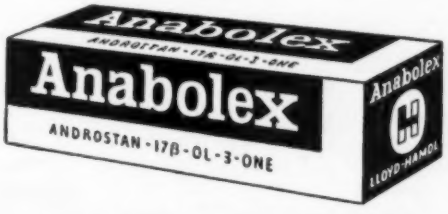

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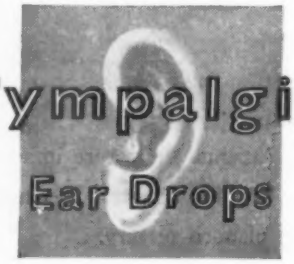

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aged 7 was therefore 4.3%, as against 2.9% in Paulett and Tuckman's 677 children under the age of 21. Hallgren made a detailed inquiry into the social factors.

In his second study, Hallgren[2] examined the clinical, social, and genetic aspects of 213 cases of nocturnal enuresis severe enough to have been referred to the psychiatric out-patient department of a paediatric hospital or as in-patients to a children's psychiatric ward. Of these, 15% were onset cases, with a significantly higher proportion of girls than of boys. Emotional stress (disturbance of the relationship between mother and child, or unsatisfactory home) seemed to be connected with the onset especially when the child also showed diurnal enuresis. This finding is in accordance with my own observations at the Mersham Reception Centre, where the high incidence of reported enuresis on admission (32% of those over 3 years of age) seemed closely related to their unsatisfactory home conditions. Whether the familiar improvement that rapidly occurs when "deprived" children are happily settled in suitable homes is restricted to onset cases has not been determined.—I am, etc.,

London, S.W.13. HILDA LEWIS.

REFERENCES

[1] Hallgren, B., *Acta psychiat. neurol. scand.*, 1956, **31**, 379.
[2] Ibid., 1957 Suppl. 114.

Munchausen Syndrome

SIR,—I must congratulate Drs. J. C. Barker and T. G. Grygier (*Journal*, November 22, p. 1274) on their lucid description of six cases of Munchausen's syndrome. I have only one small correction: it was a horse doctor, not a house doctor, who is alleged to have operated on Elsie Packoma[1]—an experience much more typical of Baron Munchausen's adventures.

It is interesting that every one of these patients has been at this hospital within the last few years, because this shows that the apparent commonness of the syndrome is an illusion caused by a very few cases visiting a very large number of hospitals. Putting it another way, in the last five years nearly every hospital doctor has met two or three cases of Munchausen's syndrome, but during that time very few people have met any other cases except those listed by Drs. Barker and Grygier. Never in the history of hospitals have so many doctors been so much annoyed by so few patients.—I am, etc.,

Central Middlesex Hospital, London, N.W.10. RICHARD ASHER.

REFERENCE

[1] Asher, R., *Lancet*, 1951, **1**, 339.

Sex Education for Students

SIR,—With Dr. Edward J. R. Rossiter's excellent letter on the above subject (*Journal*, November 8, p. 1164) I am in complete agreement. But the implementing of Dr. Rossiter's suggestions poses I think a number of problems. If students are to receive sex education, what will they be taught, and by whom?

Recently, probably stimulated by the controversy over the Wolfenden Report, I read a number of books and articles on homosexuality, and I can only say that I was quite appalled by the lack of even an elementary knowledge of sexual physiology and psychopathology displayed by the writers. One of these authors cited, as a typical case of "neurosis supervening on homosexuality," a young man who felt sexually attracted to girls but who was unable to have irregular unions with them on account of an earlier warning by his mother and his subsequent "fear of making them pregnant." Was this such a very abnormal reaction? Was it in fact a neurosis at all, or merely the very normal reaction of a sensitive and morally sound young man? And, instead of this patient being told that his reaction was both normal and understandable, he was apparently dismissed as an intractable homosexual.

The treatment, too, offered to these unfortunate people was almost negligible. A minute percentage was selected for Freudian analysis, which nearly all the writers, with two exceptions, found disappointing. Very strangely, too, continence seemed to be advised only "if it did not seem likely to lead to neurosis," otherwise it was not advised. But in not one single instance did any author advise *mental continence*, or any attempt by the patient to control his sexual fantasy-life, which of course must be the beginning and foundation stone of all attempts to reach sexual maturation. Nor, again, was there a single attempt by any author to teach the patient that his sex life must eventually (for any normality or stability) be linked with and dependent upon his tender emotions, which must always be his sole guide to any sex-expression, and that such a linking may require (if he really wants to reach maturity) months of abstinence, self-sacrifice, complete abolition of fantasies, and a sustained desire to allow the growth of all tender sentiments regarding the opposite sex.

Therefore, while I endorse the ideal set forth by Dr. Rossiter, I am greatly at a loss to know how it could be achieved. Sex education which is based upon utterly wrong premises is probably much worse than no education at all. It is proverbially much more difficult to teach a person who has been badly taught than one who knows nothing about the subject.—I am, etc.,

Planer, Middlesex. ROBERT THOMPSON.

Costs of Notification

SIR,—I should like to point out to Drs. E. O. Gibson and R. M. Emrys-Roberts (*Journal*, November 15, p. 1229) that the saving from the abolition of fees for notification of diseases might not be great. For all moneys earned by G.P.s outside the Pool, a corresponding deduction is made from the Pool. So, if fees from notifying diseases ceased, a corresponding increase would take place in the Pool, and this, unlike notification fees, would count as pensionable income.—I am, etc.,

Devonport. J. LAWRENCE HENRY.

SIR,—I feel that the letter of Dr. E. O. Gibson and Dr. R. M. Emrys-Roberts (*Journal*, November 15, p. 1229) concerning notifications has put this subject into its proper perspective. A recent experience of mine shows how farcical the whole thing can become. While working in a hospital in England, I was responsible for the medical care of the staff. My opinion was asked as to whether a cleaner whose child had scarlet fever should continue her duties. I advised that she should, provided that she had no symptoms and was not working in the children's ward. The following day the hospital secretary received a message from the M.O.H. passing on the notification. I therefore contacted the M.O.H. and stated the position. The outcome of this was that the M.O.H. insisted on the woman remaining at home during the period of infection.

Pondering on this rather drastic move, I can see only two logical conclusions. One is that sore throat should be made notifiable and treated in isolation; this is surely absurd. The alternative is to delete scarlet fever from the list of notifiable infectious diseases. I feel that this move is long overdue and would strongly support the plea that it should be done as soon as possible.—I am, etc.,

Edinburgh, 10. BRYAN ASHWORTH.

Blood Groups in Cyprus and the Near East

SIR,—I read with great interest your leading article on blood groups in Cyprus and the Near East (*Journal*, October 18, p. 959) in which it is said: "Nothing is known of the Rh groups in this area" (Syria and Lebanon). I have studied this question in Beirut with Dr. J. Mouacdie.[1]

We found the following incidence of Rh negatives: 4.4% for Moslem Arabs; 6.4% for Armenians; and 7.0% for Christian Arabs.—I am, etc.,

Beirut, Lebanon FARID S. HADDAD.

REFERENCE

[1] Haddad, F. S., and Mouacdie, J., *Lebanese med. J.*, 1951, **4**, 200.

Combined Gastric and Duodenal Ulceration

SIR,—I was most interested to read the paper by Dr. R. Mangold in your issue of November 15 (p. 1193), confirming most of my findings reported in 1955[1] and 1956,[2] particularly in regard to the great frequency of haemorrhage

and other complications in patients with combined ulcers. However, there is one point on which we have differed. This is the matter of the importance of gastric retention in the pathogenesis of the gastric ulcer, which, we both agree, is nearly always secondary to the duodenal ulcer.

Dr. Mangold recorded an incidence of 9.2% of cases of frank pyloric stenosis in his own series (28% when minor evidence suggesting obstruction was included). He concluded "pyloric stenosis does not appear to be a major factor in the pathogenesis of combined ulcers." But frank pyloric stenosis is only the final stage of a slowly developing lesion, and radiology is too crude a method to detect the earlier stages, many of which are surely almost certainly present as well in any series containing a number in the final stage. Dr. Mangold's own figures imply that the proportion of his own patients with some degree of pyloric obstruction was substantial, even if he does not accept the belief held by many that active duodenal ulcers always cause some degree of functional pyloric obstruction. Frank organic stenosis is quite a different matter and develops slowly over the years. Either kind of pyloric obstruction, or indeed, gastric retention from any cause, can promote a secondary gastric ulcer—I have given reasons and examples in the papers referred to. My view was further supported by the finding of often unsuspected associated gastric ulcers in a substantial proportion of patients known to have pyloric obstruction from another cause.

Royal Free Hospital, London, W.C.1. H. DAINTREE JOHNSON.

REFERENCES

1 Johnson, H. D., *Lancet*, 1955, **1**, 266.
2 —— *Surg. Gynec. Obstet.*, 1956, **102**, 287.

Marie Stopes

SIR,—By arrangement with the executors of the late Dr. Marie Stopes we have commissioned Mr. Keith Briant to write her official biography. We shall be most grateful if any of your readers who possess letters from Dr. Stopes, or who could provide personal recollections of her, would be kind enough to make them available to Mr. Briant through us. All original documents will be carefully copied and returned without delay.—I am, etc.,

IAN PARSONS,
Chairman,
The Hogarth Press.
40, William IV Street, London, W.C.2.

SIR,—I am writing a book about the character, life, and struggles of the late Dr. Marie Stopes. Any help from your readers in the form of letters, reminiscences, press cuttings, or any other relevant information would be most gratefully received. Any items lent will be treated most carefully and returned promptly, and may be sent to me either at the address below, or care of my publishers, Messrs. Barrie Books Ltd., 3 and 4, Clement's Inn, London, W.C.2.—I am, etc.,

ELIZABÉTH SMART.
9, Westbourne Terrace, London, W.2.

POINTS FROM LETTERS

Hazards of Sport

Dr. K. E. JOLLES (West Bromwich) writes: Dr. E. Brauer states (*Journal*, November 22, p. 1296) that he has seen more fatalities amongst spectators than players of football. That it is, certainly, not always the combatant who dies was forcibly brought home to me on an occasion earlier this year when I was officiating as medical officer at a "speed hill climb" competition. A driver had successfully and quite creditably completed his three practice runs as well as his two competition ones and, his task of the day done, had repaired to the paddock to watch his fellow competitors. An hour later, whilst thus engaged in "spectating" quietly, he suddenly collapsed and died almost instantaneously of coronary thrombosis. The interest of this case lay in the fact that this man had actively competed earlier that day and suffered no ill-effect, but died an hour later whilst watching others.

Obituary

A. HOWARD CUTTING, M.B., B.S.

The tragic death of Dr. A. Howard Cutting in a car accident on the evening of November 25 was a great loss to the general-practitioner service of south Cambridgeshire. The death of his wife, Margery Cutting, at the same time was a sad and bitter blow not only to the family but also to the village of Balsham, in which they lived.

Educated at King's College School, Wimbledon, Alfred Howard Cutting, who was born on December 28, 1914, proceeded to London University and King's College Hospital, graduating M.B., B.S. in 1939. He served as a house-surgeon at King's and also as clinical assistant to the department of urology and as resident medical officer at St. Luke's Hostel. At the outbreak of war in 1939 he was attached to the Emergency Medical Service and served in it until he joined the R.A.F. in 1940. Here he proved not only his medical worth but also his ability to turn his hand to other skills. He was for a long time with a squadron in Gibraltar and also served in North Africa, as well as at stations in England.

Dr. A. BROWN writes: In July, 1946, Dr. A. Howard Cutting joined a practice based on Linton in south Cambridgeshire, and was a partner there when he died. During the twelve years he helped to build up a group practice and became not only the doctor but the counsellor and friend of the patients. The technical knowledge of building which he possessed was invaluable when the group practice centre was being built. He will be greatly missed in Balsham, where he took a great interest in village affairs. The regard and esteem in which he was held not only by the patients but also by the medical profession were evidenced by the very large congregation which was present at the funeral service in Balsham Church.

Although not medically qualified, Dr. Margery Cutting was before her marriage doing work directly connected with medicine, and she obtained the degree of Ph.D. for her work on the sulphur content of food. She was awarded a Beit Memorial Fellowship at Cambridge and worked under and with Professor R. A. McCance before and after her marriage. She took a great interest and a very active part in the village life and also in the Women's Institute and the work of the Girl Guides in the district. She will be sorely missed by all with whom and for whom she worked. To both sets of parents and to the three young sons who are left we all extend our most sincere sympathy.

Mr. JOHN HESKETH writes: I first met Dr. A. Howard Cutting when he was a squadron medical officer in the R.A.F. in 1943. Being more senior and experienced, Flight-lieutenant Cutting (as he then was) became my guide, counsellor, and friend in all matters of a Service nature. My association continued for some 18 months as our respective squadrons kept fairly close together, and he was always willing to help in any way he could. He had already been on an overseas posting, and when my turn came nothing was too much trouble to him in advising or instructing me in every possible detail. I still have in my possession a "primus" stove in working order which he personally modified for my use. Although a doctor, he could, I found, turn his hand to things other than medicine, and in later years I came to realize how much of a handy-man he was, particularly in respect of houses, boats, and cars. It was not until 1948 that chance again threw our paths together, by which time he was established in general practice near Cambridge. Over the last 10 years he and his family and mine have remained friends, and at all times I have found him eager to help others and always of a cheerful disposition. He could not tolerate inefficiency, particularly when rules and regulations were involved, and

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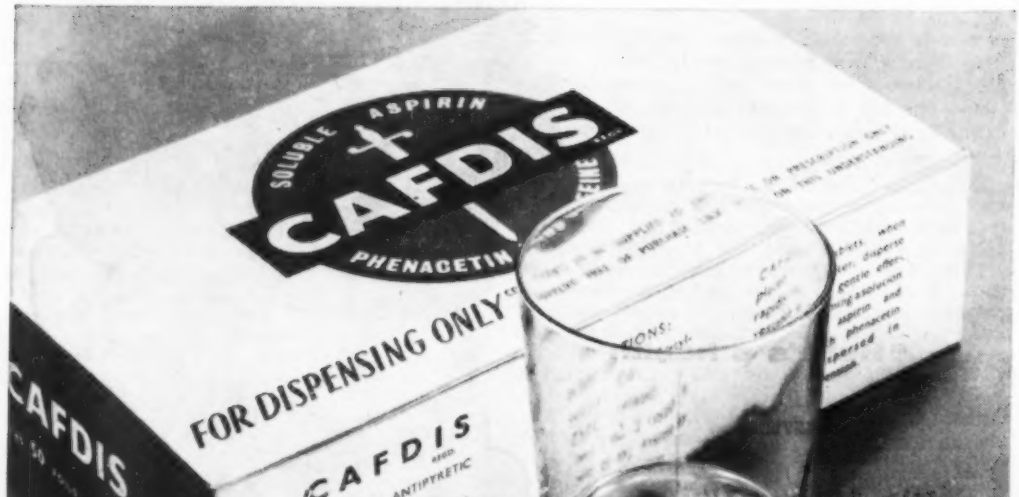

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he never lost an opportunity to bring anything of this nature to light, especially if the occurrence had been to the detriment of his patients. Although somewhat dogmatic in his clinical approach, he was in every sense a conscientious general practitioner. Outside medicine, sailing was a hobby which gave endless delight both to himself and to his family. By his untimely death his colleagues, and particularly his own village of Balsham, have lost a very dear friend. The death of his wife at the same time was another bitter blow to the family. Three young sons are left, and to them and the parents of the deceased our deepest sympathy is extended.

T. C. CLARE, M.D., F.R.C.S., F.R.C.O.G.

Mr. T. C. Clare, who was honorary surgeon to the Leicester Royal Infirmary for many years, died on November 12 at the age of 77.

Thomas Charles Clare was born in Birmingham, where his father was city treasurer. From King Edward's School he went on to study medicine at Birmingham University and St. Bartholomew's Hospital, qualifying in 1905 and graduating B.S. a year later. After being house-surgeon to Mr. Jordan Lloyd at the Queen's Hospital, Birmingham, he later became resident medical officer under Sir John Bland-Sutton at the Chelsea Hospital for Women. In 1909, the year he came to Leicester, he obtained the F.R.C.S. and proceeded to the M.D. (London) in gynaecology in the following year. For three or four years he was in single-handed general practice, and in 1913 he was appointed to the honorary surgical staff of the Leicester Royal Infirmary. At the outbreak of the first world war he joined the R.A.M.C. and served in the 5th Northern General Hospital at Leicester until 1916, when he was sent out to Mesopotamia. While there he contracted sandfly fever and dysentery and was transferred to Bombay to convalesce, spending the next two years in the North-West Frontier Province. It was there that he did his original work on the effect of heat on the red blood corpuscles, later publishing his paper "On the Toxic Nature of the Stroma of the Red Blood Corpuscles." It was characteristic of him that he did most of the experimental work on himself. As a result of this work he devised a method of treatment of certain bacterial infections. Some years after resuming his work at the Leicester Royal Infirmary he published a paper on "Gastromyotomy—an Operation for the Cure of Chronic Gastric Ulcer." He became president of the Leicester Medical Society in 1929 and read his address on "The Physiology of Cancer." After working for two or three years as honorary secretary of the Leicestershire and Rutland Division of the B.M.A., he was its chairman in 1932–3. In 1938, the year he was elected F.R.C.O.G., he delivered his presidential address to the Midland Obstetrical and Gynaecological Society, giving it the title "A Socratic Dialogue on Cancer." He had previously given a paper to this Society on "The Keloid Ovary," basing his hypothesis on clinical and physiological evidence. Although he was due to retire in 1941, he carried on until the end of the war, and his appointment was further extended owing to the rather long illness of a colleague, so that ultimately he gave 39 years' service to his hospital. He is remembered with great admiration and affection by a long line of house-surgeons, several of whom have achieved distinction. Among doctors' families he was in great demand as an obstetrician and gynaecologist.

In his younger days Mr. Clare was a keen cricketer and rugby player, but in later years his chief recreations were golf, fly-fishing, bridge, and reading. He possessed a very fine and extensive library. It gave him great pleasure when in 1937 he was elected captain of the Leicestershire Golf Club, a position which he held until 1941. Four years later he became president and was eventually elected a life member as a tribute to his great popularity. He was a Freemason of 40 years' standing. Unassuming modesty and charm were the outstanding characteristics of his personality which endeared him to his colleagues, nursing staff, and patients alike. He possessed a fine original mind and had the unique faculty of expressing *multum in parvo*. Our deepest sympathy is extended to his wife and only son, the Rev. Thomas Charles Hunter Clare.

M. W. PATERSON, O.B.E., *M.C.*, M.R.C.S., L.R.C.P.

Dr. M. W. Paterson, who was in general practice at Hyde, Cheshire, for nearly thirty years, died at Llandudno Hospital on November 15. He was 71 years of age.

Matthew Wallace Paterson was born at Tinsley, Yorkshire, on September 3, 1887, and was educated at Glasgow High School and Manchester Grammar School. He went on to St. John's College, Cambridge, where he took his B.A. in 1908. Receiving his clinical training at Manchester Royal Infirmary, he qualified M.R.C.S., L.R.C.P. in 1913, and then held the appointments of house-surgeon at Alnwick Infirmary and at Manchester Royal Infirmary and senior resident medical officer at Hope Hospital, Salford. On the outbreak of the first world war he joined the R.A.M.C., and served with distinction in France, attaining the rank of major. He was awarded the Military Cross in 1917 and was appointed O.B.E. in 1919. He was also decorated by the French Government, receiving the Médaille d'Honneur, with crossed swords. After the war he settled in Hyde, where he remained for the whole of his working life, taking an active part in local medical affairs. He was chairman of the Hyde Division of the B.M.A. in 1930–1, and had served on a number of Headquarters committees. When the Association held its Annual Meeting at Manchester in 1929 he acted as one of the honorary secretaries of the Section of Occupational Diseases, and in the following year he was honorary secretary of the Association of Certifying Factory Surgeons. Rheumatoid arthritis and overwork entailed his retirement from practice in 1947, when he moved to Drayton Parslow, Buckinghamshire, where he lived until a month or two before his death.

F. V. G. P. writes: "Pat," as Dr. M. W. Paterson was known in Hyde, had a charming personality and inspired great affection in patients and friends alike. His patients loved him, knowing that they could be sure of his interest and sympathy, and that he would do all he could to help them. As a young man he was an excellent hockey player, but his real love was for fishing and he spent many hours on the banks of the Dove, in Derbyshire. He was also a keen amateur painter. For the last 30 years of his life rheumatoid arthritis limited these pleasures to a great extent and made his work increasingly tiring and difficult. During all this time he was devotedly helped by his wife, who acted as his chauffeuse for many years, and nursed him to the end. Our sympathy goes out to her, and to his son and daughter.

H. S. ROBERTS, M.D.

Dr. H. S. Roberts, formerly one of Southport's oldest practitioners, died at a nursing-home at Wilmslow, Cheshire, on November 9. He was 84 years of age.

Hubert Shearwood Roberts was born on May 23, 1872, the son of Dr. A. Morton Roberts, of Sheffield. He received his medical education in North America, graduating M.D. from New York University in 1895. After a period as house-surgeon at the Bellevue Hospital, New York, he went on to obtain the Toronto degrees of M.D., C.M. in 1896, and then returned to the United Kingdom to take the Scottish triple qualification in 1897. After working for some time as a ship surgeon he settled at Southport in 1900 and was in practice there until he retired to Wilmslow two years ago. In addition to the work of his practice he assumed a heavy list of public duties, being medical officer to several convalescent and children's holiday homes. During the first world war he served as a captain in the R.A.M.C. in Belgium and France and, later, on recruitment boards. As president of the Southport Medical Society in 1922 he gave an address

on the doctor's car, a subject on which he could speak with some authority. Chairman of the Southport Division of the B.M.A. in 1923–4, he also represented his Division at the Annual Representative Meeting from 1944 to 1947, and was often seen at other Annual Meetings. His death came after a year of ill-health, and he is survived by his wife and a son and daughter. In manner quiet and courteous; in appearance dignified (his dress perhaps a little reminiscent of Edwardian days); assiduous in the care of, and loved by, his patients; devoted to his family—surely the verdict must be "Well done."—W. A. M.

Medical Notes in Parliament

DEBATE ON WOLFENDEN REPORT

The House of Commons put aside its party lines on November 26 to give expression to its opinions on the Report of the Wolfenden Committee on Homosexual Offences and Prostitution. It was asked to do no more on this occasion than "take note" of the report.

Mr. R. A. BUTLER, Leader of the House as well as Home Secretary, in the opening speech put the debate on a serious, human, and at times troubled level. He suggested that the delay of 12 months or so since the report was presented had given a useful opportunity for reflection; and was the first of many speakers to comment that the two parts of the report had not very much to do with one another.

Homosexual Conduct

Their main concern, Mr. BUTLER told the House, would be to decide whether the committee's recommendations for changes in the law were to be accepted. The essence of Mr. Butler's argument was this: the Wolfenden Committee drew a sharp and valid distinction between sin and crime; while private homosexual conduct between consenting adults was commonly regarded as a sin, it ought not to be a crime. The argument that if conduct that was morally wrong was not injurious to society it should be left to the operation of the individual conscience was impressive; but it could be accepted as a reason for leaving homosexuality to the private conscience only if one was convinced that society would not be harmed by so doing. An impression had gained ground, unfair to the Wolfenden Committee, that they desired to legalize homosexual conduct. In fact, what they wished to do was to remove these practices, like adultery and other sins, from the realm of the law. It was clear, however, that there was at present a very large section of the population who strongly repudiated homosexual conduct and whose moral sense would be offended by an alteration of the law which would seem to imply approval or tolerance of what they regarded as a social evil. Therefore the Government were satisfied that they would not be justified, on the basis of opinions expressed so far, in proposing legislation to carry out the committee's recommendations. The committee had drawn attention to the need for research, and, with a reservation related only to heavy demands already imposed on the Home Office, he undertook to follow up the committee's desire.

Legislation on Prostitution

On prostitution, there was probably little disagreement on what was desirable; the question was—what is practicable? Here the principal recommendation was that the law should be reformulated in three ways. The first was to eliminate the requirement to establish annoyance. He thought that was right. The second was that the maximum penalty should be increased, and the system of progressively higher penalties introduced, culminating in sentences of three months' imprisonment for a third and subsequent offences. He had no doubt of the need to clean up the streets. The Wolfenden Committee had made a strong case for its recommendations, and he could now see the lines on which legislation giving effect to them would be framed. That legislation was being prepared. He was predisposed to sympathize with the view that it was inequitable that the woman should be punished and the man should not. But practical considerations presented real difficulties: the man normally did not loiter; it was not his persistent presence, but that of the woman, that was offensive or injurious; it was almost impossible to identify the man, but it was comparatively easy to identify the woman. It was, further, most important that the law should not be framed in terms that would expose an innocent woman to any danger of arrest for alleged loitering or soliciting. Any new definition of the offences must satisfy two criteria: it must not expose an innocent woman who behaved indiscreetly to arrest; and it must not impose on the police an impossible burden of proof.

On the section of the report relating to living on immoral earnings, Mr. Butler rejected the conclusions as not firm enough and accepted the reservation of three women members that the maximum penalty should be raised to five years' imprisonment. Finally he spoke about the findings on premises used for prostitution, and confessed that on this he did not at present see a way of providing a reasonably speedy and effective remedy that would not at the same time do harm to innocent subtenants.

Dr. Broughton and Dr. Bennett

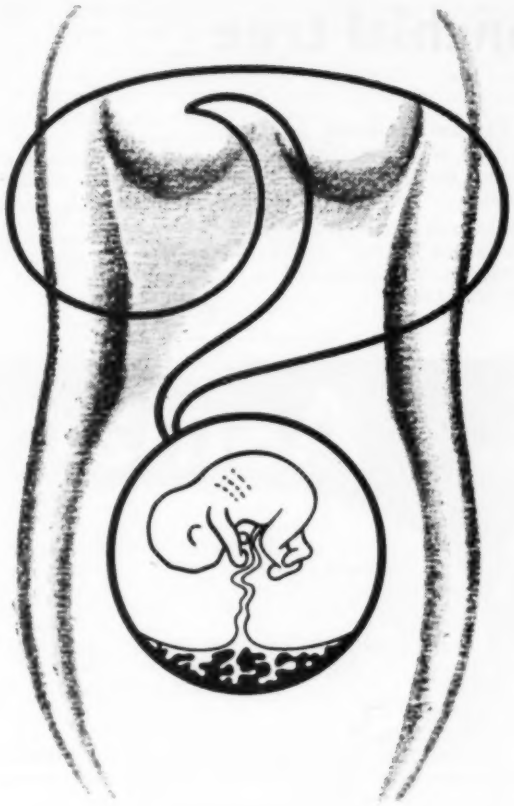
Two doctors, both with experience of psychiatric work, but as it so happened on opposite sides of the House politically, took part in the debate, and both were opposed to the Wolfenden recommendations on homosexuality.

Dr. A. D. D. BROUGHTON (Batley and Morley, Lab.), after expressing some surprise that the Wolfenden Committee had been asked to investigate two vices so very different, said that he had less knowledge of prostitution because few prostitutes went to psychiatrists. He understood that the psychiatrists who gave evidence regarded prostitution as a social problem and did not supply the committee with any helpful advice. He could see their point of view; but it must be recognized that there was something psychologically abnormal about a woman who chose that way of earning a living. Those whom he had met professionally were women who had been deprived of the love of one or both parents in childhood. He agreed with a view that had been expressed that they were incapable of giving or receiving love. Those he had come across all suffered feelings of isolation and worthlessness. But it would be wrong to generalize from so few cases. There was need for a great deal more research, including research into the mentality of men who resorted to prostitutes. The sight of prostitutes in the streets was displeasing to respectable men, offensive to respectable women, and a thoroughly bad example and temptation to the young. For those reasons he agreed with the recommendations of the committee. But they would not be effecting a cure.

Half a Million Male Homosexuals

Some authorities put the prevalence of homosexuality among males as 4%, others as low as 2%. At the lower figure it would mean that there were half a million male homosexuals in the British Isles. The causes were deeply embedded in a person's mental make-up. Undoubtedly in some cases there were constitutional factors, but it was believed that the environment and upbringing of a child were the most important factors. Normal sexuality was part of the process of growing up, but there were some people in whom the natural process of development was arrested and even reversed.

The homosexuals who took the male or active part appeared of the masculine type. He believed they had been directed along the path of homosexuality by accident: for example, they might in childhood have been made to avoid girls, and therefore have come to regard them with repulsion; or they might, as boys, have had sexual experience with an adult woman and that had filled them with some feeling of disgust. Others had a femaleness



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* *Medicine Illustrated, July 1956, p.475*

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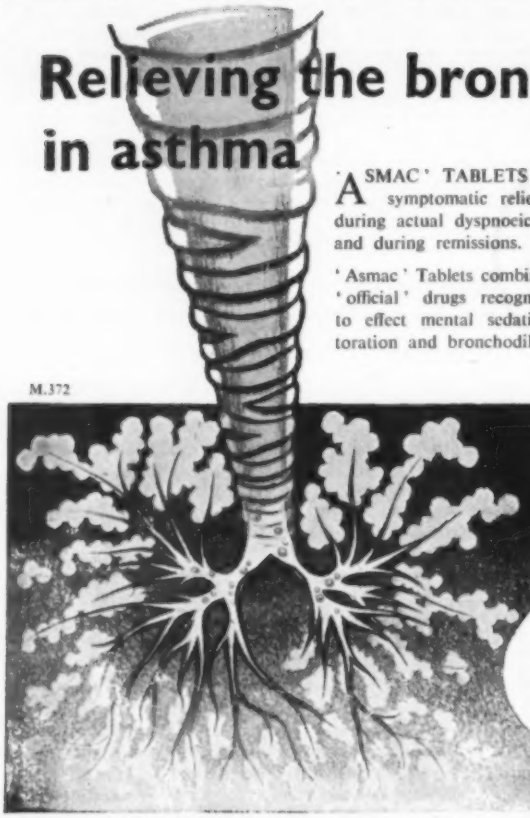

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Caffeine B.P.	0.10 g. (1.54 grains)
Theophylline with Ethylenediamine B.P.	0.15 g. (2.31 grains)

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Since its introduction over two years ago, 'DAPTAZOLE' Brand of Amiphenazole has become firmly established as an adjunct to morphine in the treatment of intractable pain.

'DAPTAZOLE' does not appreciably diminish the analgesic action of morphine, but shows a marked and lasting antagonism to the respiratory and narcotic depression.

A report on 'DAPTAZOLE' concerns the treatment of **127** cases of the terminal stages of carcinoma with severely painful lesions. Large doses of morphine were given with 'DAPTAZOLE' and total relief of the pain was achieved in almost all cases.

REFERENCES
1. *Nature*, 1955, *175*, 388.
2. *B.M.J.*, 1956, *1*, 142.
3. *B.M.J.*, 1955, *1*, 1367.
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5. *Schweizerische Medizinische Wochenschrift*, 1956, *38*, 1100.
6. *Practitioner*, 1957, *179*, 1071.

'DAPTAZOLE' for concurrent use with morphine is available in the following packs:

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of outlook: they probably had a bad father-image, and because of it had more interest in what the mother and sisters were doing. This type were vain and apt to indulge in exhibitionism. It was in that group that were found the really decadent types and the male prostitutes.

It was true, to a large extent, that it was possible for homosexuals to repress their desires. But the sex urge was not weakened in a man by his being a homosexual. Treatment was extremely difficult. Many homosexuals looked upon the suggestion of becoming heterosexual as quite absurd. It must be realized that it entailed changing their whole life pattern. He agreed with an intervention by Dr. DONALD JOHNSON (Carlisle, Con.) that hormone treatment merely lowered sexuality in general rather than making any change in homosexuality.

Legal Sanctions

The question to be decided was: should the law be modified in the way recommended by the Wolfenden Committee—namely, that homosexual practice among consenting adults should no longer be a criminal offence? If the recommendation was accepted, the general public would gain the impression that Parliament condoned this practice. Homosexuality was biologically wrong. If the recommendation was accepted he had a fear, based on what he knew of homosexuals, that some, not all, would repress their homosexual feelings less. They might go to the extent even of showing some signs of the affection they had for one another in public. He could envisage men walking along the street arm in arm, possibly holding hands, perhaps wishing to dance together, and even caressing in public places.

Mr. S. SILVERMAN (Nelson and Colne, Lab.) said that, supposing Dr. Broughton was right, was that a justification for sending homosexuals to prison, which would be the inevitable result of not changing the law?

Dr. BROUGHTON replied that the law was very savage. He thought the penalties too severe. It was a pity that such heavy penalties were ever imposed. But to alter them at this time, he feared, would be misunderstood and many people would think they were condoning these offences. He would not himself go as far as to send them to prison. Long-term imprisonment was too severe a penalty, and prison was quite the wrong place to send these people. But unless some punishment was imposed there was a danger of others becoming acquainted with the practice and indulging in it. It was a well-known fact that homosexuals banded themselves into groups, and if the law were changed so that they did not have the fear of punishment these groups might elevate the practice of homosexuality to a cult. He had heard of groups in which considerable trouble had been taken by some members in the seduction of others. He was not in favour of accepting the Wolfenden recommendations.

Dr. REGINALD BENNETT (Gosport and Fareham, Con.) welcomed the agreement of Dr. Broughton with his own views, because he felt that few other members of the psychiatric profession agreed. He had thought he was in a minority of one, but saw now that it was a minority of two. He agreed that, on prostitution, what they were trying to do was to take the advertisement of the wares of these people off the streets, even if the practice was historically insuppressible. He would certainly say that the penalties should be raised, but they must beware of doing so to such an extent that every case became defended, and the defence of the women became more and more an undertaking for the "monarchs" of the industry. They should certainly penalize very heavily those who exploited this industry, if they could be caught.

Adolescent Partners

He had done a good deal of practice at the request of the courts in reporting on the state of mind and indeed undertaking the treatment of homosexuals. In the light of his experience he found it difficult to understand why the Wolfenden Committee came to the conclusions they did. On the strength of expert witnesses, to wit psychiatrists, the report stated (para. 57):

> "We are authoritatively informed that a man who has had homosexual relations with an adult partner seldom turns to boys, and *vice versa*, though it is apparent from the police reports we have seen and from other evidence submitted to us that such cases do happen."

That might be true, though he doubted it. They should have much more information before accepting that. He declined to accept that the man who accepted an adult male as his partner would not seek an adolescent male above the age of puberty. He thought they all did. That was why, if indulgence in private was made not an offence, the House would be permitting the spread of an activity that would inevitably lead to a greater evil in proselytizing adolescents.

Mr. F. TOMNEY (Hammersmith, North, Lab.), interrupting, said that in 1947 the Cambridge Institute of Criminal Science made an inquiry covering 1,000 cases from 14 police districts. There were 275 indictable offences for homosexual practices involving 406 accomplices or victims. The majority of the victims were under the age of 16, and only 11% over 21, and only one case of one adult with a consenting adult.

Dr. BENNETT said he was sure that was not far from an average figure. He had seen a fairly large number of homosexuals and he had been struck by the proportion who were adolescents who had been picked up. They were late developers, slow in maturing, uncertain of their sexual direction, and they had been pushed into that direction. He had found it remarkably easy to cure these people with the aid of hormone treatment. This could so suppress sexual tension that a reorientation of ideas had time to take place, so that when sexual desires were allowed to return on the cessation of treatment they were in a more natural form. If patients were suitably selected it seemed that there was a good prospect of cure. That showed that they could not regard homosexuals as incurable, nor as hereditary, congenital, or even environmentally produced people who must have a separate way of life. In his belief a big part in the influencing and curing of these young men had been the fear of the sanction of the law. He would take issue with anyone who said the law was not a deterrent. It was a profound deterrent, especially in those of whom they had the most hope of success. It would be disastrous to abandon the law on that point. For these reasons he could not accept the Wolfenden findings on homosexuality. The evidence produced by the psychiatric profession could not necessarily be accepted as being as sound as it had been accepted as being by the Wolfenden Committee.

ANSWERS TO QUESTIONS

Change of Sex and Divorce Law

Mr. KENNETH ROBINSON (St. Pancras, North, Lab.) asked the Attorney-General if his attention had been called to the legal difficulties arising from the case of Dolling *versus* Dolling, recently before the Court of Appeal; and if he would consider amending the law of divorce to enable marriages to be dissolved on the grounds that a spouse had changed his or her sex. Sir REGINALD MANNINGHAM-BULLER said he was not aware of any legal difficulties. The Court of Appeal held, on the particular facts of that case, that the conduct of the respondent did not amount to cruelty. Sir Reginald did not think there was any need to amend the law by seeking to specify what acts constituted cruelty for the purposes of the law of divorce or by making express provision for the type of case mentioned in the question.

Disparity in Hospital Costs

Dr. DONALD JOHNSON (Carlisle, Con.) asked the Minister if he was aware of the wide disparity of in-patient hospital costs revealed by his department's recently published hospital costing returns, varying in the case of acute

hospitals from £16 0s. 1d. per patient per week for the Middlesbrough General Hospital to £36 9s. 1d. per patient per week for the Royal Northern Hospital, with all gradations of cost in between, showing wide differences even for apparently similar hospitals; and what he proposed to do to find the reason for, and eliminate if possible, such disparities. Mr. WALKER-SMITH replied that some variations were inevitable even in hospitals classified in the same broad category, because of differences in local conditions and in the services provided. It was, however, one of the objects of the new costing arrangements to provide a firmer basis of comparison of detailed hospital costs, and he had asked hospital authorities to make full use of the published information with a view to improving efficiency and securing economies.

Cancer Diagnostic Clinic at Bart's*

Mr. W. HANNAN (Maryhill, Lab.) asked the Secretary of State for Scotland if he was aware of the proposal to establish a clinic at St. Bartholomew's Hospital for free examination for early diagnosis of cancer; and if he would ask for full details of this project and consider taking similar action in Scotland. Mr. JOHN MACLAY: I have noted the proposal and will certainly watch its progress.

Vital Statistics

England and Wales in 1957

The infant mortality rate again reached a record low figure in 1957, being 23 deaths of children aged under 1 year per thousand live births, according to the *Registrar-General's Statistical Review of England and Wales for the Year 1957*, Part I, Tables, Medical (H.M.S.O., £1). The crude death rate was 11.5 per thousand population, and this too was a record low figure when adjustments are made for the age and sex structure of the population.

The table below contrasts crude death rates for 1947 and 1957 for certain causes of death. The large fall in the death rates for the two infectious diseases listed there is to be seen in the death rates for almost all infectious diseases, including those caused by viruses. In the composite category "Deaths attributable to viruses," for instance, the death rate was 51 in 1947 and 22 in 1957. The principal cause of death in this category in 1957 was infectious hepatitis, with a death rate of 7 per million population.

Crude Death Rate per Million Population, 1947 and 1957, England and Wales

Cause of Death	1947	1957
Respiratory tuberculosis	473	95
Whooping-cough	22	2
Cancer of:		
Stomach	335	312
Rectum	151	120
Pancreas	61	80
Lung and bronchus, males	(1943)485	759
,, ,, ,, females	(1949) 87	116
Breast, females	349	370
Uterus	193	169
Prostate	143	161
Leukaemia	35	53
Chronic rheumatic heart disease	240	183
Arteriosclerotic and coronary disease	895	1,700
Hypertensive disease	352	434
Acute bronchitis	165	63
Ulcer of stomach	71	58
,, ,, duodenum	45	53
Appendicitis	36	18
Chronic nephritis	154	76
Suicide	105	118

Scotland in 1957

At 11.9 per thousand population the general death rate in Scotland in 1957 was the lowest for 4 years, but higher than in 1953, when it was 11.5, according to *The Annual Report of the Registrar-General for Scotland for 1957* (H.M.S.O., £1). The infant mortality rate was 28.6 per thousand live births, which was the same as in 1956 and the lowest rate recorded until then.

A comparison of standardized death rates for Scotland and for England and Wales in 1957 shows that for most of the main causes of death Scotland's figures are less favourable. One of the most striking disparities is for diabetes mellitus, the death rate for which was 108 per million in Scotland and 69 in England and Wales. This disparity has increased during recent years, for in 1953 the two rates were 95 and 72. The rate for pulmonary tuberculosis was 136 per million in Scotland and 94 in England and Wales in 1957. The difference between them has remained similar since 1953, when the rates were 235 and 178 respectively.

As usual, the death rate from pneumonia (all forms) was higher in England and Wales (520) than in Scotland (445), and both these figures have increased fairly steadily since 1953, when they were 488 and 363 respectively. Hypertensive disease is also a commoner cause of death in England and Wales, the rate being 429 as compared with 392 in Scotland in 1957. In the large composite group of heart diseases, however, Scotland has the higher rate with 3,999 as against 3,378. In the other two large groups, malignant neoplasms and vascular lesions of the central nervous system, the rates for Scotland are somewhat higher than for England and Wales.

The death rate from syphilis was 20 in Scotland and 29 in England and Wales; these rates have hardly altered in the 5 years 1953–7. An increasing disparity in the death rates from rheumatic fever is notable. In 1953 the rate for Scotland was 8 and for England and Wales 7. Thereafter it did not fall below 8 for Scotland but has steadily diminished in England and Wales, so that in 1957 the two rates were 9 and 4.

18 deaths of reputed centenarians (16 verified) occurred during the year, 1 male and 17 female. The greatest number to be registered in one year is 19—in 1918 and 1950. The greatest age verified was 109 years 14 days of a person who died in 1936.

Week Ending November 22

Infectious diseases were more prevalent in England and Wales during the week ending November 22. The largest rises in the number of notifications were 333 for measles, from 5,779 to 6,112, 133 for dysentery, from 614 to 747, 113 for scarlet fever, from 975 to 1,088, 60 for acute pneumonia, from 309 to 369, and 51 for food-poisoning, from 196 to 247; the only large fall was 48 for whooping-cough, from 805 to 757.

The largest rises in the incidence of measles were 86 in Hampshire, from 81 to 167 (New Forest R.D. 58), 76 in Durham, from 86 to 162 (Stanley U.D. 62), 69 in Wiltshire, from 125 to 194 (Swindon M.B. 67), and 61 in London, from 326 to 387 (Paddington 83); the largest decreases were 56 in Worcestershire, from 96 to 40, and 55 in Buckinghamshire, from 98 to 43. The number of notifications of scarlet fever was the largest for almost 3 years; the largest rises during the week were 30 in Lancashire, from 133 to 163, and 20 in Essex, from 43 to 63. Only small variations were reported in the local returns of whooping-cough. 9 cases of diphtheria were notified, being 3 more than in the preceding week; 5 of these cases were notified in London (Finsbury 4, Hampstead 1) and 2 in Barking M.B., Essex.

4 of the 9 cases of paratyphoid fever were notified in Sussex, Brighton C.B.

The notifications of acute poliomyelitis numbered 72, and these cases were 3 fewer for paralytic and 9 more for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 14 (Bradford C.B. 2, Huddersfield C.B. 2, Leeds C.B. 2, Pudsey M.B. 2); Lancashire 8 (Manchester C.B. 4); Warwickshire 8 (Birmingham C.B. 6, Rugby M.B. 2); Derbyshire 6 (Bakewell U.D. 2); London 5 (Wandsworth 2).

The largest outbreaks of dysentery were Yorkshire West Riding 98 (Leeds C.B. 53, Thorne R.D. 15), Lancashire 91 (Eccles M.B. 49, Liverpool C.B. 14), Warwickshire 87 (Coventry C.B. 72, Birmingham C.B. 12), London 77

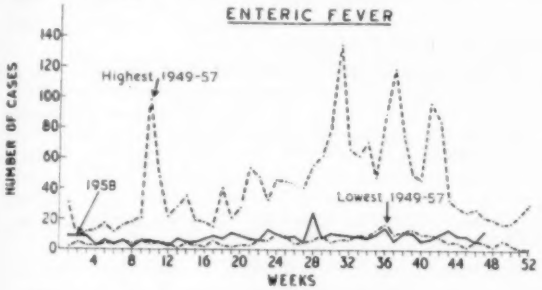
*A statement from St. Bartholomew's Hospital is printed at p. 1423.

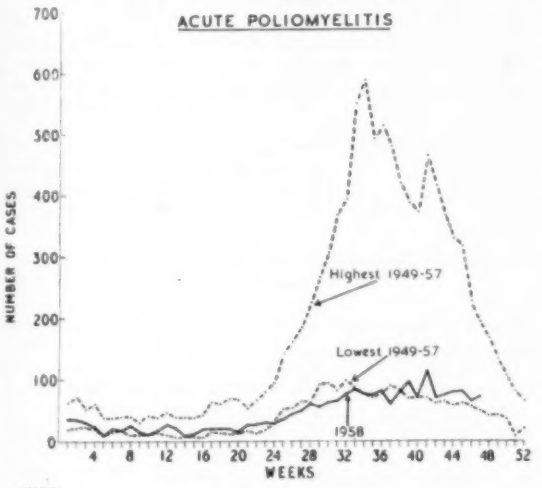
(Lambeth 20, Battersea 12, Deptford 10), Glamorganshire 48 (Rhondda M.B. 14, Cardiff C.B. 12), Cumberland 41 (Carlisle C.B. 25, Millom R.D. 16), Surrey 39 (Godstone R.D. 25, Croydon C.B. 11), Essex 32 (West Ham C.B. 13), Hampshire 27 (Southampton C.B. 14), Nottinghamshire 25, and Middlesex 20 (Hendon M.B. 14).

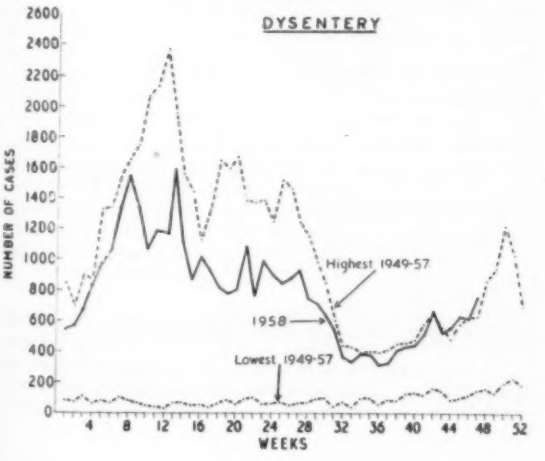
The largest outbreak of food-poisoning was 58 cases in Crewkerne, Somersetshire.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **November 15** (No. 46) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	6	1	8	0	1	5	0	2	0	2
Dysentery	614	80	141	7	4	278	29	94	11	3
Encephalitis, acute	2	0		0		3	0		0	
Enteric fever:										
Typhoid	3	0	0	0		4	1	0	0	1
Paratyphoid	3	0	3(B)	0	1(B)	15	0	0	0	
Food-poisoning	196	34	20	1		136	15	4	0	
Infective enteritis or diarrhoea under 2 years				13	25				16	26
Measles*	5,779	326	105	26	303	1,695	36	25	11	25
Meningococcal infection	18	0	9	0		24	0	10	1	2
Ophthalmia neonatorum	28	4	1	0		28	5	5	0	
Pneumonia†	309	31	180	0		623	50	293	9	53
Poliomyelitis, acute:										
Paralytic	50	4	14	3	6	55	6	2	4	1
Non-paralytic	16	0				13	0			
Puerperal fever§	197	17	8	0		220	38	7	1	
Scarlet fever	975	83	109	21	38	550	41	60	11	28
Tuberculosis:										
Respiratory	478	54	96	24		504	77	128	16	
Non-respiratory	82	9	16	1		82	8	12	3	
Whooping-cough	805	40	78	79	104	472	26	46	0	6

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	4	0	1	0	0		0	2	0	0
Influenza	16	0	1	0	0		7	13		14
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				0	0		
Pneumonia	404	37	18	17	3		53	20	15	14
Poliomyelitis, acute	3	0		0	0		1		0	0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	93	8	13	1	4		8	12	1	8
Non-respiratory		2	0	0	0		1	0	0	0
Whooping-cough	1	0	0	1	0		0	0	0	0
Deaths 0–1 year	320	23	35	9	13		19	23	6	17
Deaths (excluding stillbirths)	9,444	708	599	129	148		826	565	128	215
LIVE BIRTHS	13,505	1233	968	219	311		1098	866	186	296
STILLBIRTHS	304	29	28				20	23		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

G.M.C. Centenary Dinner.—The General Medical Council held its centenary dinner at the Mansion House, London, on November 27. The president, Sir DAVID CAMPBELL, received the many distinguished guests, who included VISCOUNT KILMUIR, the Lord Chancellor. In proposing the toast of the G.M.C., Sir HAROLD GILLETT, Lord Mayor of London, said that the Council could be described as characteristically English, for it was born in Parliamentary compromise and operated as a compromise. It was not a Government department, yet the Crown nominated eight members; nor was it a voluntary association. In reply, Sir DAVID CAMPBELL sketched the Council's achievements over the last 100 years in improving the education, ethics, and social status of the profession of medicine. "To-day I am proud to think that the attainments of the general practitioners in these islands are higher than anywhere else in the world," he said. Such was the prestige of the British *Register* that last year almost a thousand practitioners from all parts of the Commonwealth sought to have their names inscribed thereon. Sir David said it had been very gratifying to receive the following message from the Vice-Chancellor of an Indian University:

"The General Medical Council has played a vital role in the development of Medical Education not only in the British Isles but throughout the Commonwealth. If we have been able to achieve the present standard of medical education in India, it is largely on account of the guidance that we received from the General Medical Council and the British universities."

Lord COHEN OF BIRKENHEAD, who toasted the guests, welcomed particularly the representatives of the Medical Councils of the Commonwealth and Burma. The reciprocity and temporary registration which enabled practitioners from other countries to work in Britain, and practitioners from Britain to work in the Commonwealth, provided an abiding link of friendship. Speaking as the present head of a sister profession, the Law, Viscount KILMUIR congratulated the Council on the manner in which it dealt with its disciplinary work. "In this mad century and in the odd world in which we have lived," said the Lord Chancellor, "a body that has kept the old, tried, and valued conception of natural justice before it, and has gained respect in its application, can think worthily of itself and of its labours."

Richard Bright Centenary.—The centenary of the death of Richard Bright (1789–1858), physician to Guy's Hospital, was commemorated at Guy's Hospital Medical School on December 1. During the afternoon a number of cases were shown at a combined clinical round illustrating the theme of chronic Bright's disease, attended by many distinguished guests. Dr. W. N. MANN, director of the department of medicine at Guy's, who introduced the round, pointed out the difficulty of establishing the aetiology in many cases of chronic Bright's disease, even after necropsy. He also commented on the rarity of chronic glomerulonephritis, having been unable to find an example in Bright's own hospital for the afternoon's demonstration. After tea Professor M. L. ROSENHEIM delivered the Bright Centenary Lecture before a large audience. Professor Rosenheim discoursed on the syndrome of Bright's disease—which was what Bright had described—rather than a disease entity. He reviewed the remarkable advances made in the investigation of renal disease, and showed how aortography might occasionally uncover abnormalities of one kidney, which could lead to the syndrome of chronic Bright's disease but, if remedied early, offered hope of complete cure. In thanking Professor Rosenheim, Professor ROBERT PLATT said that not only had they heard a brilliant lecture but one by a clinician which would have pleased Richard Bright himself. During the day an exhibition arranged by Dr. C. KEITH SIMPSON was on view in the Gordon Museum. Amongst the many exhibits were the original specimens of the kidney examined by Bright, a copy of *Reports of Medical Cases*, as well as writings by Bright outside the subject of medicine, and a copy of the original number of the *Guy's Hospital Reports*. In the evening a dinner was given by the Medical School at the Royal College of Physicians, under the chairmanship of Dr. A. C. HAMPSON.

Chair of Medicine, Manchester.—Dr. D. A. K. BLACK is to succeed Professor ROBERT PLATT, P.R.C.P., in the chair of medicine at Manchester University, according to a report in the *Manchester Guardian* (December 2). Dr. Black is the present reader in medicine at Manchester. "Professor Platt," states the report, "has asked to be relieved of his full-time chair of medicine and directorship of the department because of his duties as President of the Royal College of Physicians. Dr. Black graduated B.Sc. at St. Andrews in 1933 and M.B., Ch.B. in 1936, proceeding to the M.D. with honours and the Rutherford gold medal in 1940. He was admitted M.R.C.P. in 1939 and elected F.R.C.P. in 1952. Before going to Manchester Dr. Black was a Beit memorial research fellow at Oxford and Cambridge. In 1953 he was Goulstonian lecturer of the Royal College of Physicians.

Royal College of Obstetricians and Gynaecologists.—At a meeting of the council on November 29, with the president, Professor A. M. CLAYE, in the chair, the William Blair-Bell memorial lectures for 1959 were awarded to Dr. WINIFRED J. A. FRANCIS and Dr. M. L. PATERSON; and the Green-Armytage short-term travelling scholarship for 1959 to Dr. J. C. S. LEVERTON. Congratulations were sent to Professor J. M. MUNRO KERR for his 90th birthday anniversary on December 5.

Feversham Committee.—Mr. R. F. D. SHUFFREY, secretary of the Departmental Committee on Artificial Insemination (Home Office, Whitehall, London, S.W.1), writes: "The committee would welcome the views of any member of the medical profession who may be interested in this subject, and I should be grateful if anyone who is prepared to assist the committee in this way would get in touch with me at the above address." The committee is asked to inquire into the existing practice of human artificial insemination and its legal consequences; and to consider whether, taking account of the interests of individuals involved and of society as a whole, any change in the law is necessary or desirable.

Halliwick Hospital.—On November 27 the DUCHESS OF KENT opened Halliwick Hospital, London, N.11, said to be the first post-war hospital in the London area built specifically for psychiatric purposes. It is a 152-bed unit adjoining Friern Hospital. It cost £260,000 and took two years to build. The Ministry of Health described it as representative of the modern approach to psychiatry—"active treatment of early cases and their quick return to the community." Halliwick Hospital will take, by informal admission, short-stay neurotic patients and patients in the early stages of psychoses. The hospital will be closely linked with community services in its catchment area. Besides providing conventional in-patient facilities, it will also act as a "day hospital" for patients who return to their homes at night after treatment and will allow for evening out-patient treatment of those working during the day. The medical superintendent is Dr. I. SUTTON.

Nuffield Lecture Fund.—The council of the Royal Society of Medicine has accepted from Lord NUFFIELD a sum of £3,513 to establish a Nuffield Lecture Fund. This is the balance of contributions from doctors to an eightieth birthday tribute to Lord Nuffield (see *Journal*, December 28, 1957, p. 1558). The Fund will provide for periodical lectures on the advancement of the science and art of medicine.

Anaesthetist Registrars Prize.—The Scottish Society of Anaesthetists offers a prize of £30 to an anaesthetist not above senior registrar grade for an essay, full particulars of which may be obtained from Dr. M. SHAW, honorary secretary of the Society, at 75, Woodend Drive, Glasgow, W.3.

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Mental Health Manual.—The British Red Cross Society has produced a *Mental Health Manual* written by Dr. D. STAFFORD-CLARK, of Guy's Hospital, and illustrated by Miss SYLVIA TREADGOLD. The manual aims at giving "the essentials of a first-aid and nursing approach to all types of illness in which psychological disturbance plays an important part." In part I the author discusses some aspects of normal psychology and describes mental development from infancy through adolescence to adult life. In the second part he shows how this knowledge can be put to use in the care of the sick patient. In a third short part he gives advice on psychological first aid following a major disaster, such as a railway accident, flood, or attack in war. The manual is obtainable from the Society at 14, Grosvenor Crescent, London, S.W.1, for 3s. (3d. postage).

Burden Neurological Institute.—Professor F. L. GOLLA, director of the Burden Neurological Institute, Bristol, since 1936, is retiring. He will be succeeded by Dr. W. ROSS ASHBY, at present director of research at Barnwood House, Gloucester.

Cytology Service at Bart's.—A question was asked in Parliament on November 25 about a cancer diagnostic clinic at St. Bartholomew's Hospital (see p. 1420). The hospital has issued this statement.

"The setting up of a cytology service for the early diagnosis of cancer at St. Bartholomew's Hospital is at present under discussion between the Corporation of London and the Governors of St. Bartholomew's Hospital. A statement giving details of the scheme will be issued, although it may be some time before the service can come into operation."

French Medical Film Prize.—The annual prize for 16-mm. medical films offered by *La Presse Médicale* (value 100,000 francs) will be awarded at the Nouvelle Faculté de Médecine de Paris on March 17. Entries and films should be sent to *La Presse Médicale*, 120, Boulevard Saint Germain, Paris, 6, before February 15.

Sir Walter Mercer has had conferred on him the honorary fellowship of the Royal College of Surgeons in Ireland.

COMING EVENTS

Institute of Dermatology.—Semi-permanent exhibition, December 3 to 30, on "The Skin and Friction."

B.B.C. North Home Service.—"Doctors on Trial," December 10, from 10 to 10.30 p.m.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, December 6

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Addenbrooke's Hospital, 10.30 a.m. and 2.30 p.m., symposium: Blood Diseases and Reticuloses. Morning: The Malignant Reticuloses. Papers by Dr. D'A. Kok and Drs. E. M. Kingsley-Pillers and F. G. J. Hayhoe. Afternoon: The Common Anaemias. Papers by Dr. F. G. J. Hayhoe and Mr. S. J. Hopkins.

Sunday, December 7

CAMBRIDGE UNIVERSITY MEDICAL SCHOOL.—At Radiotherapeutic Centre, Addenbrooke's Hospital, 2 p.m., symposium. Papers by Dr. Janet Roscoe, Dr. B. B. Zeitlyn, Dr. C. H. Whittle, and Dr. G. V. Balmforth.
EUGENICS SOCIETY.—At Royal Society, Burlington House, W., 5.30 p.m., Dr. J. A. Fraser Roberts: Human Genetics at Two International Conferences.

Monday, December 8

GUY'S HOSPITAL.—At Anatomy Lecture Theatre, 5.15 p.m., lecture-demonstration in endocrinology by Dr. P. M. F. Bishop: Diabetes Insipidus.
LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., special university lecture in pathology by Dr. B. Josephson (Stockholm): Examination of Renal Function in Man by Renal Vein Catheterization.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Guest lecture by Professor H. Scarborough: Purpura.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4 p.m., Harben Lecture by Sir Samuel P. Bedson, F.R.S.: Psittacosis-Lymphogranuloma Group of Infective Agents—(1) History and the Characters of these Agents.

Tuesday, December 9

ASSOCIATION OF ANAESTHETISTS OF EDINBURGH.—At Surgeons' Hall, Nicolson Street, 7.45 p.m., Dr. C. T. Barry and Dr. J. D. Robertson: Halothane.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. L. Forman: Disturbances of Pigmentation.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. H. Lander (Adelaide): Kuru (The Laughing Disease)—A Recently Discovered Disorder of the Central Nervous System.
MANCHESTER MEDICAL SOCIETY: SECTION OF SURGERY.—At Clinical Sciences Building, York Place, 7.30 for 8 p.m., Mr. H. M. Goldberg: Lesions of the Fundus of the Gall Bladder; Dr. J. R. Edge: Use of Steroids in Major Surgery for Debilitated Patients with Advanced Tuberculosis.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. W. S. C. Copeman: Medical Practice in the Tudor Period—Evolution of the Profession.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Erasmus Wilson Demonstration by Dr. L. W. Proger: Aneurysms.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4 p.m., Harben Lecture by Sir Samuel P. Bedson, F.R.S.: Psittacosis-Lymphogranuloma Group of Infective Agents—(2) Position of the Agents of Trachoma, Inclusion Conjunctivitis and Cat-scratch Disease. The Ecology of the Agents of the Psittacosis-Lymphogranuloma Group.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. Aleck Bourne: Influence of the Emotional Factor in Gynaecology.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. N. G. Hulbert: neurological demonstration.
WEST OF ENGLAND CHILD HEALTH GROUP.—At Department of Child Health Lecture Theatre, Children's Hospital, Bristol, 8.30 p.m., Professor A. V. Neale: A Recent Tour Abroad.

Wednesday, December 10

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Precancerous and Cancerous Conditions of the Skin.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. Donald Barlow: Surgery of Pulmonary Tuberculosis Viewed in Perspective.
● INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Guest lecture by Mr. C. M. Gwillim: Anatomy of Prolax.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. A. R. Harrison: Tests of Renal Function.
MANCHESTER MEDICAL SOCIETY: SECTION OF PATHOLOGY.—At Large Anatomy Theatre, Manchester University, 4.30 for 5 p.m., Dr. B. Sandler: Testicular Biopsy; Its Interpretation and Value in Infertility.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Guest lecture by Dr. B. Josephson (Stockholm): Renal Blood Flow Determinations in Man.
ROYAL COLLEGE OF SURGEONS OF EDINBURGH.—3.30 p.m., Mr. D. J. Waterston: Abnormal Development of the Heart and its Surgical Correction.
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW.—5 p.m., Lock Lecture by Sir Eric Riches: New Growths of the Kidney.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—4 p.m., Harben Lecture by Sir Samuel P. Bedson, F.R.S.: Psittacosis-Lymphogranuloma Group of Infective Agents—(3) Diagnosis, Treatment, and Control of Infection of Man with these Agents. The Taxonomic Position of the Group.

Thursday, December 11

HONYMAN GILLESPIE LECTURES.—At Anatomy Theatre, University New Buildings, Teviot Place, Edinburgh, 5 p.m., Mr. A. B. Wallace: Thoughts on Wound Healing and Wound Care.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. W. S. C. Copeman: Medical Practice in the Tudor Period—Growth and Status of Medical Practice.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Bradshaw Lecture by Sir Archibald McIndoe: Problem of Facial Burns.
ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION, PSYCHOTHERAPY AND SOCIAL PSYCHIATRY SECTION.—At 11, Chandos Street, W., 8 p.m., Dr. R. F. Hobson: Analytic Attitude in Psychiatry.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., Professor P. C. C. Garnham and Dr. D. J. Lewis: Parasites of British Honduras, with Special Reference to Leishmaniasis. A discussion will follow.
ST. ANDREWS UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Professor Dugald Baird: Practical Importance of Clinical Research in Obstetrics.

Friday, December 12

BIOCHEMICAL SOCIETY.—At Department of Biochemistry and Chemistry, Medical College, St. Bartholomew's Hospital, 2 p.m., 378th meeting.
CAMBRIDGE UNIVERSITY POSTGRADUATE MEDICAL SCHOOL.—At Radiotherapeutic Centre, Addenbrooke's Hospital, 4 for 4.15 p.m., clinical and clinico-pathological meeting. Discussion to be opened by Dr. A. J. Rook: Melanoma and its Precursors.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. E. H. Hudson: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., special lecture by Professor W. St. C. Symmers: Mycotic Diseases.
KEIGHLEY AND DISTRICT MEDICAL SOCIETY.—At Victoria Hospital, Keighley, 8.30 p.m., Dr. P. M. Addison: The Law as it Affects the Doctor.
KENT AND CANTERBURY HOSPITAL.—8 p.m., clinical meeting.
PLYMOUTH MEDICAL SOCIETY.—At Greenbank, 8.30 p.m., clinical evening.

Sunday, December 14

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—10.15 a.m. to 12.30 p.m., Seminar for General Practitioners by Mr. C. Gill-Carey: Common Ear, Nose, and Throat Conditions.
MANCHESTER UNIVERSITY: FACULTY OF MEDICINE AND NORTH-WEST ENGLAND FACULTY, COLLEGE OF GENERAL PRACTITIONERS.—At Theatre 1, Clinical Sciences Building, York Place, 11 a.m., Professor E. W. Anderson: Arteriosclerotic Encephalopathy.

BIRTHS, MARRIAGES, AND DEATHS

DEATHS

Clare.—On November 12, 1958, Thomas Charles Clare, M.D., F.R.C.S., F.R.C.O.G., of 19, Central Avenue, Leicester.
Davenport.—On November 15, 1958, Edward Charles Davenport, M.B., of 19, Kirkdale Road, Harpenden, Herts, aged 87.
Eminson.—On November 19, 1958, at 2, Burringham Road, Scunthorpe, Lincs, Ralph Franklin Eminson, D.S.O., M.B., B.S., aged 69.
Guppy.—On November 13, 1958, at The Grove House, Church Stretton, Salop, Francis Henry Guppy, *M.C.*, M.R.C.S., L.R.C.P., D.P.M.
Miles.—On November 10, 1958, at St. Thomas's Hospital, London, S.E., Tudor Miles, M.B., B.S., D.Obst.R.C.O.G., of The Spurriers, Horsell, Woking, Surrey.

Any Questions ?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Linoleic Acid and Coronary Atheroma

Q.—*Does "arcofac" (linoleic acid, pyridoxine HCl, mixed tocopherols) have any beneficial effect on existing atheroma of the coronary vessels?*

A.—There is no direct evidence that the administration of linoleic acid has been beneficial to patients with atheroma of the coronary vessels. There is evidence that in animals atheroma can be produced by a diet high in saturated fatty acids and can be prevented by linoleic acid. There is also evidence that in man a diet containing unsaturated fatty acids from vegetable oils such as corn oil, peanut oil, or olive oil leads to a decrease in serum cholesterol, whereas butter, eggs, and beef fat increase it. There is, however, no direct proof that high serum cholesterol levels lead to atheroma in man. Further evidence linking coronary disease with a high consumption of animal fats comes from statistics of the incidence of coronary thrombosis in various countries and groups of people; there is strong evidence of an association, though this does not necessarily imply a causal relationship. This evidence has led some workers to urge strongly that the consumption of more unsaturated fatty acids and less saturated fats should prevent the development of coronary disease; other workers, however, contest this conclusion. The subject is fully discussed in several articles in the *British Medical Bulletin*,[1] which were the subject of an annotation in the *Journal* (October 18, p. 963).

REFERENCE

[1] *Brit. med. Bull.*, 1958, **14**, 197-278.

Amphetamine Sulphate and Preludin

Q.—*In view of the close similarity in chemical composition between amphetamine sulphate and preludin, why has the former been made a "scheduled" drug and not the latter?*

A.—There is indeed a very close similarity in chemical composition and mode of action between amphetamine sulphate and preludin. That the former has been made a "scheduled" drug and not the latter is probably due to the fact that amphetamine has been available for some time and a considerable experience has accumulated, not only of its possible advantages, but also of its dangers and drawbacks. The undesirable effects of preludin, which probably closely approximate to those of amphetamine, have not so far been as thoroughly appreciated. There is a honeymoon period for most new drugs, and perhaps preludin has not as yet settled down into humdrum married life.

Ringworm

Q.—*What are the indications for x-ray epilation of the scalp in ringworm due to microsporon infection? Is exclusion from school necessary?*

A.—Children with small-spore ringworm of scalp should be excluded from school because of the risk of epidemic spread. If after cultural examination the fungus is found to be *Microsporum canis*, the condition may be expected to clear spontaneously or readily following the application of fungicides. It is important that infected contacts and animals should be dealt with at the same time. Very rarely *Microsporum canis* infection does not clear with such treatment. Infection with *Microsporum audouini* may similarly clear spontaneously, but in a large proportion of cases is resistant to fungicidal treatment, which should, however, be tried for two or three months. It is these persistent cases of *Microsporum audouini* which call for *x*-ray epilation of the scalp.

NOTES AND COMMENTS

P.A.S. and Pulmonary Tuberculosis.—Dr. M. O. J. GIBSON and Dr. M. M. NAGLEY (London, S.E.12) write: We wonder if we could be granted the courtesy of your columns to protest at the answer to the question regarding the effectiveness of Ca B-P.A.S. as opposed to sodium P.A.S. ("Any Questions?" November 8, p. 1174). Your expert maintains that evidence is difficult to obtain regarding the relative values of the two substances and goes on to quote, *in extenso*, a paper in which weighty conclusions are drawn following an analysis of a mere seven cases treated with Ca B-P.A.S. The author of this paper[1] does us the honour of extensively quoting our original paper[2] dealing with this very matter, in which more than two hundred cases treated with Ca B-P.A.S. were analysed, in which the conclusions drawn were that Ca B-P.A.S. seemed to be no less effective than sodium P.A.S. in delaying the emergence of isoniazid-resistant strains when used in combination with isoniazid. In view of the fact that your expert quoted only the most recent paper—that is, that of Lewis—we feel that our original paper should be drawn to the attention of your readers so that the papers and the results may be compared. Briefly, Sir, we would assert that there is no evidence that in clinical use Ca B-P.A.S. is inferior to any other sort of P.A.S. from the point of view of isoniazid resistance, and our follow-up of a three-year period on this very point, proving it to our satisfaction, is in the press and about to be published in another journal. Ca B-P.A.S. is extensively used in this country, and it is therefore important to try and establish its place in the treatment of pulmonary tuberculosis, and we would respectfully suggest, Sir, that this cannot be done on the lines set out by your expert, but can only be done by perusal of the available evidence.

REFERENCES

[1] Lewis, D. O., *Tubercle* (*Lond.*), 1958, **39**, 247.
[2] Gibson, M. O. J., and Nagley, M. M., *ibid.*, 1955, **36**, 209.

OUR EXPERT replies: I was, of course, aware of the early paper by Drs. Gibson and Nagley which showed that the administration of calcium B-P.A.S. with streptomycin or isoniazid for the relatively short period of two to four months was followed by the emergence of only a few resistant organisms. However, very much longer periods of treatment are now known to be essential to the effective treatment of pulmonary tuberculosis, and so far as I know the paper by Lewis is the only one which at present gives evidence about the emergence of resistant organisms in patients treated for a more prolonged period with combinations including calcium B-P.A.S. The emergence of resistant strains in three out of seven patients who were known to have had sensitive organisms at the beginning of treatment, and in 20 out of the total of 39 who were investigated but in whom the evidence about initial sensitivity was not so good, is strong evidence of which cognizance must be taken unless it can be controverted. The publication of any further evidence dealing with the rate of emergence of resistant strains in patients treated for periods of a year or more with combinations including calcium B-P.A.S. will be awaited with great interest.

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